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The Massachusetts Medical Society

The next Annual Meeting of the Massachusetts Medical Society will be held in Boston.

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The Massachusetts Medical Society

SECTION OF PEDIATRICS

Crystal Room, Hotel Bancroft, Worcester, Mass.
Monday, June 4, 1934, 2:30 P. M.

PRESIDING:
Dr. Gardner N. Cobb, Worcester, Chairman.
Dr. James M. Baty, Boston, Secretary.

CHAIRMAN COBB: The meeting will come to order. We will grant that perhaps the full quota is not here.

If no one has any objections, we will have no minutes of the last meeting read at this time. I hear no objections.

The next matter of business which is customary (I do not assume this duty) is for the Chair to appoint a committee of three, who will consult some time in the near future and appoint for the next meeting a Chairman and a Secretary, and I appoint at this time Dr. Richard M. Smith, Dr. Fritz B. Talbot, and Dr. Frederick H. Allen. If there is no objection, we will assume that this Committee is to serve us for the coming year.

There is a little elasticity allowed but the regulations require us, according to the By-Laws, to limit every paper to 20 minutes and the discussion to five minutes per person. For the sake of the stenographer, it is requested that each discusser, before he announces his subject, give his name and address.

Is there anything further to be considered before we take up our program? For this program, I may say, we are indebted to Dr. James M. Baty. I might add that we have a fifth matter to be brought to your attention, one which has been worked up by the Worcester Polytechnic Institute on the gas bacilli. We do not dare to say whether it is bacillus Welchii or bacillus aerogenes capsulatus; in fact, they do not call it one or the other; but it shows what occurs in commercial and Grade A milk, and there has been no displacement so far in our certified milk. At a convenient time this afternoon Dr. Smith will come in and will give us a five minutes' talk on this subject.

We are glad to welcome you here. The first paper is by Dr. Warren E. Wheeler, of the Massachusetts General Hospital, on "The Use of the Ketogenic Diet in Chronic Pyuria." Dr. Wheeler.

DR. WARREN E. WHEELER: *Mr. Chairman, Ladies, and Gentlemen*—I should like to turn your consideration for a few moments to the treatment of chronic pyuria in children. Chronic infection of the urinary tract not infrequently persists after the acute stage of so-called pyelitis has passed. This infection often proves very refractory to the present-day methods of treatment and constitutes a very real problem to the pediatrician. It is toward this group of cases that the following remarks concerning a new and apparently better method of treatment will be directed.

THE USE OF THE KETOGENIC DIET IN CHRONIC PYURIA*

A Preliminary Report

BY JOHN M. RECTOR, M.D.,† AND WARREN E. WHEELER, M.D.†

THE application of chance observation has led to the discovery of many of our most valuable therapeutic measures. Among the most recent examples of this has been the development of a method for sterilizing the infected urinary tract, which appears to be far superior to those formerly in use. Several years ago, Helmholz observed that a specimen of urine from an epileptic patient who was being treated on a ketogenic diet remained perfectly clear after standing in the laboratory for a week. Subsequent bacteriologic investigation showed that organisms of the colon-typhoid group were markedly inhibited in their growth by such urines, and that many samples were actually bactericidal. This action was much less marked for staphylococcus and streptococcus than for Bacillus coli. These findings led to the trial of the ketogenic diet in the treatment of urinary infections, and in 1931 Clark[3] reported two cases so treated in adults, and Helmholz[10] reported two cases in children with infection superimposed upon congenital anomalies of the urinary tract. Since then there have been a number of case reports in the American and English literature of chronic pyelitis and chronic pyelocystitis benefited by this means. Few of these case reports are accompanied by definite statements concerning the length of time the authors were sure their patients continued to be free of symptoms.

It had long been known that highly acid urine was inhibitory to the growth of the colon bacillus. It was found, however, that although the ketogenic diet caused the excretion of acid

*Read before the Section of Pediatrics of the Massachusetts Medical Society, at its Annual Meeting, Worcester, June 4, 1934.

†Rector, John M.—Formerly Assistant Resident in Pediatrics, Children's Hospital, Boston. Wheeler, Warren E.—Formerly Resident in Bacteriology, Children's Hospital, Boston. For records and addresses of authors see "This Week's Issue," page 187.

urine, one could not duplicate the inhibiting action on bacteria shown by these urines by acidifying normal urines to the same degree. Nor could one attain this effect by the addition of acetone and diacetic acid, even in acid urine. Helmholz[14] has shown that the inhibiting effect tends to wear off after patients have been on the diet for a period of ten days or more. Other workers have shown that individuals vary greatly in their ability to excrete bactericidal urine, and that the same urine may exercise a different degree of inhibition toward the various species of the colon-typhoid group of organisms causing urinary infection. About a year ago, Fuller[8], in England, proved that the effectiveness of urines from patients on ketogenic diets was directly proportional to the amount of beta oxybutyric acid present, this acid being the major ketone body in these urines. He showed very conclusively also that beta oxybutyric acid was effective only when the urine was highly acid, i.e., having a pH of 5.5 or lower.

Both the laboratory data and clinical impressions, then, point to several factors which must be taken into consideration if one hopes to clear up a chronic urinary infection which has proved refractory to the ordinary methods of treatment. In the first place, the infection must be caused by an organism easily inhibited by the ketone urine; secondly, one must obtain quickly a urine containing an abundance of ketone bodies; thirdly, the urine must be highly acid; and fourthly, it should be as concentrated as possible.

The course of a child with chronic pyelitis or chronic pyelocystitis successfully treated by this régime is little short of spectacular. After placing the child on the diet, there is usually a period of a day or so before adequate ketosis develops and acetone bodies appear in the urine in sufficient concentration to be effective. With the development of ketosis, practically all the complaints of urgency, frequency, incontinence and burning on micturition stop abruptly, although in the urine one may demonstrate as many pus cells and bacteria as before. This sedative action on the bladder mucosa is certainly one of the most striking features of the treatment and is seen as regularly in those cases which ultimately fail as in those which become and stay sterile. By the second or third day of ketosis, the bacteria in the urine, which may have numbered five or ten million per cubic centimeter at the outset, diminish remarkably, and in four or five days the urine usually is found to be sterile. The children commonly lose a pound or more in weight during the first few days on the diet, but this should not be disturbing, as rapid weight gain occurs when the normal diet is resumed.

Clinical trial in this country and abroad has indicated quite clearly the types of cases in which the best results may be expected. In the first place, it should be realized that the management of a successful ketogenic régime in no way compares in simplicity with the dispensing of pills, and unless one is dealing with an exceptional home situation, hospitalization for two or three weeks is practically imperative. Consequently if the infection can be cleared with intensive treatment by the usual methods, there is little justification for subjecting the patient to two or three weeks of a ketogenic régime. The very nature of the ketogenic diet cautions against its use in the presence of fever. In the treatment of infection superimposed upon congenital anomalies, different workers have reported widely varying results. Practically all investigators are agreed that every case of chronic pyuria in childhood deserves a thorough study to determine the presence of any anatomical factor which may aggravate the condition or hinder its cure, and have advocated surgical correction of the deformity whenever possible. Helmholz[11] has reported excellent results in the dietary treatment of these cases, but other workers, including ourselves, have failed to obtain permanent benefit from such treatment. In addition, we have failed to produce sufficiently intense ketosis to accomplish sterilization in those cases of advanced pyelonephritis where the renal function, as determined by the phenolsulphonephthalein test, has been greatly impaired.

In our hands, and this has been the experience of the majority of workers, the most gratifying results with the dietary treatment have been obtained in chronic cystitis, and chronic or recurrent pyelonephritis in the absence of congenital anomalies of the urinary tract. Certainly it is in these cases, especially when the more accepted measures have failed, that a trial on the ketogenic diet is justified.

The ketogenic régime which has proved so successful differs but little from that which has been more or less widely used in the treatment of epilepsy in children. Most children are thrown into ketosis easily by high fat, low carbohydrate diets, and they seem to tolerate such diets very well in general. Such a diet is not generally to be recommended in children under two years of age. On account of the difficulty in preventing children from eating small amounts of carbohydrates aside from their meals, ketosis may be difficult to maintain. This problem can be met in part by raising the ratio of fat to carbohydrate in the diet. It should be emphasized again that the antiseptic properties of urines from children on such diets are apt to wear off after about two weeks. For these reasons it should be our aim to establish intense ketosis as soon as possible and to have the urine sterile before it loses its beneficial effect. To this end, the child should immediately be placed on a diet having a ketogenic-antiketogenic ratio of 3:1, and no hesitancy should be shown in in-

creasing this ratio to 4:1 or 5:1 or more if the ketosis tends to decrease. By the term ketogenic ratio of 3:1 is meant a ratio in the diet of three grams of fat to every gram of carbohydrate and protein combined. A few children will become nauseated with the high fat diet, and may vomit once or twice during its induction. The omission of the next meal in these cases will usually suffice to bring back the appetite and to prevent subsequent vomiting. The partial starvation will tend to enhance the ketosis. Such vomiting, unless it persists, is no indication for abandoning the diet.

It will be found that the child's natural tendency will be to select the carbohydrates from his tray and leave the fatty foods, and with this in mind, it will be found easier to induce ketosis if the child is underfed rather than overfed. About twenty calories per pound is sufficient to carry the child through the short period of treatment, raising the ratio if necessary in preference to the total caloric intake. A typical 3:1 diet for a three-year-old child weighing thirty-five pounds would contain ten grams each of carbohydrate and protein, and sixty grams of fat, this 3:1 ratio being maintained at each meal.

Fluids should be limited as much as the child's disposition will permit after ketosis develops. It is quite feasible and possible to restrict the fluids of a three-year-old child to 600 cubic centimeters a day, and of a nine-year-old child to 800 cubic centimeters a day, and by so doing to enhance the antiseptic properties of the urine tremendously.

To our knowledge, there is no practical clinical test for beta oxybutyric acid. However, it has been shown that the concentration of this acid fairly closely parallels that of acetone and diacetic acid in the urine, so that an abundance of these ketone bodies may be assumed to indicate that the effective principle is present in satisfactory amount. To make sure of the effectiveness of the diet the urine should be tested every morning for acetone or for diacetic acid, as well as for pH.* Most workers have found it necessary to give ammonium chloride or some other acidifying salt to lower the urine acidity to its effective level, i.e., to a pH of 5.5 or lower. However, in our experience, we have found it unnecessary to acidify the urine further when the fluids have been markedly restricted.

It should be emphasized that sterility of the urine should be the criterion of benefit rather than the absence of pus cells, and it will be found of great value in determining the efficacy of the treatment to take cultures every two or three days. By this means, one will know when the urine becomes sterile, and recurrences in the infection due to a lapse in the ketone content or the acidity of the urine can be determined. Even though cultures often become sterile after three or four days, clinical experience has shown the probability of recurrence of the infection when the treatment is stopped before the cultures have been sterile for at least a week.

*We have used Rothera's sodium nitroprusside test for acetone, and methyl red as an indicator for pH determinations.

In the past year, we have had occasion to follow bacteriologically on the wards and in the out-patient department of the Children's Hospital in Boston fourteen cases of chronic urinary tract infection treated by the ketogenic diet. Only those cases were selected in which the infection had lasted from two months to six years, with an average duration of about two years. Practically all of them had received more or less intensive therapy previously, with little, or only temporary benefit. All but one case, which was treated in the out-patient department entirely, remained on the ward for a period of several days for intensive study before the dietary treatment was begun. During this period of observation, all cases were subjected routinely to blood non-protein nitrogen determinations, renal function tests by the phenolsulphonephthalein method, tuberculin tests, Wassermann tests, and urine culture, and to cystograms and intravenous pyelograms (Neo-skiodan) where indicated. Thus the presence or absence of anatomical deformities, the status of the kidney function, and the absence of tuberculous infection were determined. The diet was instituted only in those cases which were essentially afebrile. The average duration of the diet was fifteen days.

Of these fourteen cases, eight became sterile during the course of the dietary treatment and remained sterile for six months, or as long as we were able to follow them. In two of the fourteen cases, we were unable to produce a satisfactory ketosis, and sterilization was never effected. It is interesting to note that both of these children had demonstrable anatomic deformities of their urinary tract. In two other cases, the urine was sterile on discharge from the hospital, but the infection recurred later. These two children, alone in our series, resumed a normal diet as soon as the cultures became negative. In no case where the patient was kept on the diet for a week or longer after the cultures became negative has there been a recurrence to our knowledge. In one case we were unable to produce a satisfactory ketosis in the hospital. Later by using a higher ratio diet and by restricting fluids at home, the urine became sterile, but the infection recurred four months later. One case was sterile on discharge, but would not return for bacteriologic follow-up. These results are strikingly in agreement with most of those reported in the literature.

In conclusion, we should like to repeat several cautions emphasized by Clark[6], and to mention a few of our own:

1) Do not expect good results in infection caused by organisms other than those of the Bacillus coli group.

2) Do not be disappointed if the infections in the presence of anatomic deformity, or advanced pyelonephritis with impaired renal function do not clear up satisfactorily.

3) Do not expect good results unless the diet is completely adhered to. Ninety per cent adherence will not give 90 per cent results.

4) Do not expect good results unless the pH of the urine is constantly less than 5.5.

5) Do not expect good results unless acetone or diacetic acid appears in the urine in large amounts on daily test.

6) Do not fail to raise the ketogenic ratio of the diet if ketosis appears to be diminishing in the first few days.

7) Do not overfeed. Twenty calories a pound is high enough to start on in children. A small diet will lead to fewer difficulties in getting the child to take it well, and will lead to a more prompt ketosis.

8) Do not discontinue the diet if the patient feels nauseated or vomits at the outset. A short period without food will probably relieve the symptoms.

9) Do not resume normal diet until the cultures have been negative for one week.

10) Do not fail to follow each case culturally—accept continued sterility as the final criterion of benefit. Pus may continue to be present in the urine for weeks after sterility occurs even in cases which do not recur.

Time and further intensive trial of this régime will be needed to prove the true value of the ketogenic diet in the treatment of bacilluria, and this preliminary report is presented with the realization that only after prolonged bacteriological study can the benefited cases be called cured. We do know that in the majority of cases we have obtained prompt symptomatic relief and that the urines have remained consistently negative to cultural and microscopic examination. However, chronic pyelitis is notably subject to natural remissions, and it is our plan to report the status of these cases in detail at the end of a period of one and one-half or two years. By this means only can the permanent benefits of the treatment be learned.

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DISCUSSION

CHAIRMAN COBB: The discussion will be opened by Dr. Fritz B. Talbot, Boston.

DR. FRITZ B. TALBOT: *Mr. Chairman*—I want to congratulate Dr. Wheeler on his fine piece of work, in the first place, and on his presentation, in the second place.

Anything that will help us in treating chronic pyelitis is, of course, of great value, and I am sure this method of treatment is a valuable adjunct to the other methods in common use. The ketogenic diet is used in certain clinics in the treatment of epilepsy, and there are practical features of its use that should be emphasized.

We are familiar with the sudden application to a patient of the high fat diet recommended here, and we have come to the conclusion that it was quite difficult suddenly to change from a normal diet to this diet. The normal diet has a ratio of about one gram of fat to about three or four grams of carbohydrate, plus protein. The sudden change in ratio to three grams of fat and one gram of carbohydrate plus protein is very marked and sometimes results in acute digestive upsets. Because of that, it has been the habit in treating epilepsy with this diet to make more gradual changes.

The problem is somewhat different in epilepsy because the time element does not play such a part as it does in the treatment of pyelitis. The possibility that Dr. Wheeler mentioned, of upsetting the stomach with such a sudden increase in fat, is real, and it takes the greatest clinical skill to prevent digestive upsets.

There is one type of case, in my opinion, that should not have the diet changed suddenly in that manner. That is the child with an enlarged liver. Such children are quite easily upset by fat.

The high fat diet is not a diet that can be prescribed by anyone. I have seen it prescribed without suitable directions, and in consequence it has gone into bad repute. Some patients have come to my office who have told me that they were on a ketogenic diet and they never had a diet which was ketogenic. The use of the ketogenic diet needs special knowledge. It needs knowledge of the caloric values of the foods as they are given, knowledge of the fat, carbohydrates, and protein content, and it is a real job to make out a ketogenic diet. It takes us at least a half hour's figuring in our office to make out the diet.

After we have handed the diet to the patient or the person who is to give it, there again can come many mistakes. One of the first mistakes is that

they do not know the composition of the foods they are given. They are told to use cream. Well, it must be 40 per cent cream, and they go and buy 40 per cent cream and then find on analysis it is only 20 per cent cream, and so forth. Careful checks should be kept on all the foods used.

More interesting and amusing incidents have come up. Among them was one child that was on, so far as I could tell and so far as the excellent trained nurse that was on the case could tell, a ketogenic diet, and yet she did not give the test for ketones in the urine. The nurse observed every mouthful that that child ate, which she had weighed and yet that child did not develop the ketosis. Finally, it was found that the child liked to brush her teeth alone in the bathroom, and she ate each morning a complete tube of sweetened tooth powder, which prevented the action of the diet. When this was corrected the test for acetone in the urine appeared.

It is our belief, contrary to that of Dr. Wheeler, that when the ketogenic diet is actually given, actually taken, you cannot help but have a ketosis, and that without exception, if acetone is not found in the urine a ketogenic diet is not being taken.

This diet cannot be applied by prescription. It must be measured out by scales, just as the diabetic diet was measured out by scales before insulin came in. And I think I am repeating what Dr. Joslin used to preach a good many times: that it is only special knowledge that can actually give a ketogenic diet and see it taken. Sometimes a period of fasting of one or two meals allows the patient to take the diet without any change. On the other hand, during hot weather the diet is more difficult to apply than during cold weather. Sometimes it causes gastric or intestinal pains temporarily. They usually disappear when the bowels have moved.

I think I have taken all the time I should take. This is a very useful method, but I think it must be used with knowledge and accuracy.

CHAIRMAN COBB: Is there any further discussion of this paper?

DR. HAROLD L. HIGGINS: Several reasons have occurred to me which might explain the basis of the value of the ketogenic diet in pyuria. My experience with epileptics makes me feel that ketogenic diets are of value in some infections. The value may be in that the ketogenic diet somewhat dehydrates the body, edema is diminished, and therefore the ability of the body to overcome infection is increased. The ketogenic diet is certainly worth trying for such cases of pyuria as Dr. Wheeler has described. I am wondering if similar results would not be obtained merely by starvation.

Dr. Wheeler said that the effect of the ketogenic diet, or more exactly, the toxicity of the ketogenic urine, seemed to wear off after one or two weeks. The question arises in my mind if it is not that the bacteria have become accustomed to the Beta-oxybutyric acid medium rather than that the toxicity of the urine has been lost. In the treatment of pyelitis by the use of alkali, we give large amounts of sodium bicarbonate and the urine becomes very alkaline; in this urine the bacteria are found at first to be markedly diminished in number; it would seem that the bacteria are unaccustomed to an alkaline media; after several days of alkaline therapy, the bacteria grow in the urine as they did previously when the child was not getting soda.

Similarly, it would seem that the bacteria were not accustomed at first to a medium which contained a large amount of Beta-oxybutyric acid, but later became accustomed to it.

Dr. Wheeler is certainly right in recommending that this diet be not given to kidney cases which are febrile. When a patient is febrile there is bound to be a certain amount of cloudy swelling of the kidneys, and possible diminution of the kidney function; one kidney function that may be diminished is the ability to excrete acid; if the kidney does not excrete acid, there is danger of the acid accumulating in the blood and acidosis developing. In diabetes, when there is infection and a resulting loss of kidney function, probably from cloudy swelling, coma is to be feared. One should be certain that the kidney function is not seriously impaired before resorting to the ketogenic diet in patients with pyuria.

CHAIRMAN COBB: Is there any further discussion?

DR. HENRY HUDSON: I think it might be worth while to emphasize two points Dr. Wheeler alluded to in reference to those patients who do not have demonstrable anatomical defects. If the pyuria is based on anatomical defects, and obstruction, it is less likely, I think, that a beneficial result should come from the use of the ketogenic diet. It is more common now than it has been in the past, but still not so common as it might be, to subject children with pyuria of long duration to a thorough urologic investigation. Although Dr. Wheeler mentions the use of intravenous pyelograms and cystograms, it should be pointed out that that method of investigation is not always reliable, and that sometimes cystoscopic examination will reveal an anatomic anomaly which is not shown by intravenous pyelograms alone.

CHAIRMAN COBB: Is there any further discussion on this paper? If not, we will go to the second paper, "Present Status of Vaccination Against Tuberculosis", by Dr. Clement A. Smith of the Children's Hospital.

DR. CLEMENT A. SMITH: *Mr. Chairman, Ladies and Gentlemen*—I did not have the advantage of Dr. Talbot's criticism, and I am forced to read my paper. I have also taken the liberty of altering the title slightly, to avoid having to make a complete analysis of the present literature, which is enormous, and I am calling it "The Clinical Basis and Present Status of Vaccination Against Tuberculosis."

THE CLINICAL BASIS AND PRESENT STATUS OF VACCINATION AGAINST TUBERCULOSIS*

BY CLEMENT A. SMITH, M.D.†

THE efficacy of the measures at present in force against tuberculosis is well shown by the steady diminution in the death-rate of this disease at all ages. However, this excellent progress should not deter us either from continuing these measures or from adding to them whatever new and useful weapons may be available. There has in the last ten years been an increasing interest in the use of immunization methods in tuberculosis. It has seemed of in-

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†Smith, Clement A.—Junior Assistant Physician, Children's Hospital, Boston. For record and address of author see "This Week's Issue," page 187.

terest to present some facts on tuberculosis as seen in a children's hospital as a basis for judging the value of such procedures.

During the years 1923-1933 (inclusive), there have been 309 deaths from all forms of tuberculosis in the Children's and Infants' Hospitals of Boston. The age distribution is shown in figure 1. It will be seen that the mortality

FIGURE 1. 309 deaths from tuberculosis (all forms) at Children's Hospital, 1923-1933, inclusive, by ages.

is very high during the first year, rises to a peak in the second, then rapidly falls, until, after the sixth year, a very low level is reached. That this curve is typical of the disease in childhood may be seen from the first part of figure 2,

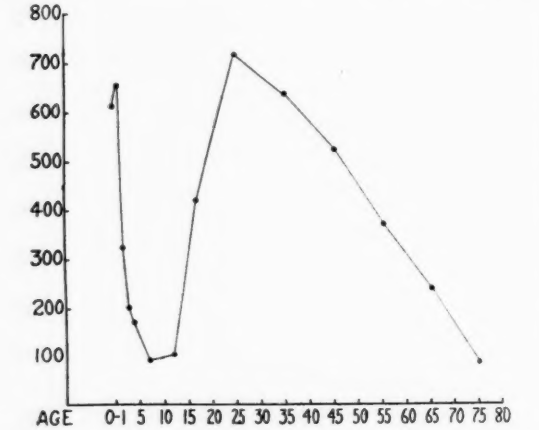

FIGURE 2. Deaths from tuberculosis (all forms), Massachusetts, 1923-1932, inclusive. Total 30,933.

which shows all the deaths from tuberculosis in Massachusetts, from 1923 through 1932. What factors are there to explain this peak of tuberculous mortality in infancy?

The most evident possibility would be simply an increased susceptibility or diminished resistance, natural to the early years of life. It is unfortunate and somewhat surprising that there have not been more studies upon this point, the assumption having been repeatedly made that babies succumb to tuberculosis largely because their age and size give them no resistance. But what investigations have been made in animals (Römer[1], Selter and Bürgers[2], Wallgren[3], and Krause[4]) have shown no difference between the response at various ages to tubercle infection. In fact, the studies of Wallgren showed a slightly greater resistance in his youngest rabbits than in any of the older groups. Until we have further evidence, we must omit the factor of age in itself as an explanation of our clinical findings.

Is the virulence of organisms infecting these infants any greater than that of organisms infecting older children? We have no reason to believe so. The majority of these children have died from the same human strain of tuberculosis which infects adults, and which must be of the same virulence. And, in spite of the opportunities for reducing bovine tuberculosis which are available to every community, a certain number of our deaths have been due to bovine organisms. We have seen such fatalities during the present year. However, although it takes its toll, the bovine strain is possibly less virulent for man—and certainly not more so—than the human type.

When we consider the factor of amount of organisms, we feel it quite probable that a larger number of bacilli may be conveyed to small infants than to older children. We have history of contact—usually familial—or of raw milk feeding, in slightly over 44 per cent of these cases. This figure could undoubtedly be raised by more careful investigation than we have been able to carry out. As milk is the major food of infants, and as familial exposure is of necessity intimate in the close physical contacts of caring for and feeding babies, we conclude that the "dosage" of organisms in many of these cases is larger than may obtain in older children.

Thus, while we consider our small children as no more susceptible by age than older individuals, they may well be infected by larger numbers of bacilli. Are there any further factors which may be deduced from our mortality?

We have plotted in figure 1 the incidence of tuberculous infection by ages, as shown by two studies. These figures are from Chadwick and Zacks[5] in Massachusetts (Von Pirquet test), and Smith[6] at the Bellevue Hospital in New York (Mantoux test on general admissions). While we have as yet no complete figures as to the incidence of positive tests at the Children's Hospital, we have no reason to believe that they would differ greatly from what these curves show. It is seen from the figure that where the curve of mortality shows a strikingly de-

scendent course, that of tuberculous infection is definitely ascendent. It would appear that the disease takes its childhood toll where it is implanted on the freshest, most uninfected soil.

We do not feel that the great bulk of mortality occurring later than childhood, when the infection rate is high, necessarily invalidates this reasoning. Tuberculosis then is a different type of disease process, and its fatalities follow a quite different course. One of the criteria for the differentiation of the childhood type of tuberculosis from the adult type is that the former is a first infection while the latter is due to a re-infection, or as it has been aptly called, a super-infection.

We may then summarize our reasoning thus far as follows:

1. A certain number of infants and small children are exposed to tuberculosis. Probably according to the size and frequency of the infecting dosage, they either succumb to it rather rapidly, or withstand it, and in so doing acquire some measure of resistance to further infection, which may be termed a relative immunity. (Why this immunity should break down in later life, unless it may be due to the internal and external strains of development and adjustment, has never been satisfactorily explained.)

2. It follows that a perfectly safe method of conferring a primary infection or, better still, its attendant benefits, to infants, might produce in them some protection against the progressive forms of the disease.

The correctness of this hypothesis is borne out by animal experimentation. That animals previously inoculated with a small dosage of an avirulent form of tubercle bacilli respond to a second, virulent infection with more resistance than fresh animals receiving this latter infection, is a proved fact of laboratory investigation. The previously inoculated animal responds not only with increased resistance but in a different manner—the altered reaction for which the term allergy was coined. It should always be remembered, however, that the resistance mentioned is not an absolute immunity. It is possible to kill an animal by re-infection, but it takes a longer time to do so, or a greater dosage, than is required in a fresh animal.

Two examples of such immunity in animals may be given. One deals with the use of the bacillus of Calmette and Guérin (BCG), the other with human organisms killed by heat; two substances which we shall mention in greater detail below. A large amount of earlier work with both living and dead organisms, such as the Rl strain of Trudeau, and the killed vaccine of Langer, might also be reviewed to the same effect. It seemed more interesting to consider only recent reports on these two methods, as they are receiving the greatest attention at present.

Birkhaug[7] reported in 1933 a series of experiments with the BCG on guinea-pigs. Omitting details, his results were as follows: Groups of guinea-pigs were inoculated with BCG by various routes, and later infected with measured amounts of virulent human bacilli. Control groups not so inoculated received the same virulent infection. After the virulent infection, the orally inoculated group showed an average survival only slightly greater than that of the controls. But the intraperitoneally, subcutaneously, and intracutaneously inoculated groups survived average periods of 304, 340, and 417 days, respectively, as against 189 days for their controls. In other words, the most successful group, those intracutaneously inoculated, lived more than twice as long after virulent infection as did their controls.

Also in 1933, Soper and his associates[8] reported the results of experiments of the same type on rabbits inoculated with heat-killed bovine organisms of the S strain. They not only used normal rabbits as controls, but also groups of rabbits inoculated with BCG and with living human bacilli. Their test infection was a virulent bovine strain injected into the cisterna magna. After this infection, the control group survived an average of 116 days, those previously inoculated with human bacilli 187 days, the BCG group 246 days, and the heat-killed 280 days. Here again, animals protected with the BCG lived more than twice as long as controls, while those protected by killed organisms lived still longer.

Thus our reasoning as to the factors underlying our experiences with tuberculosis in young, previously uninfected children, has been borne out in the laboratory. Theoretically, we should be able to reproduce in human beings the protection conferred upon animals by these measures. Practically, this may be neither wise nor feasible. In a subject which has caused so much controversy, the purposes of this report may be best served by simply stating what appear to be the facts on the two inoculation methods of the greatest present promise.

The bacillus of Calmette and Guérin is an attenuated form of the bovine type of tubercle bacillus. It was isolated originally in 1908 as a normally virulent organism. It was subcultured for thirteen years on a bile-glycerine-potato medium before it was used for human inoculation. During this period its proponents felt that it assumed the characteristics of a fixed virus of such strength as to be non-pathogenic for man and the laboratory animals. Since 1921 about a million children and adults have been inoculated with it in the hope of producing some degree of immunity to tuberculosis. Inoculation was at first performed by feeding the new-born infant with 30 mg. of the bacilli. Of late, this method has been superseded by intracutaneous injection, the com-

monly used dosage being 0.15 mg. The inoculation is given only to tuberculin-negative individuals, and after inoculation it is recommended that the recipient be kept from contact with tuberculosis until the development of a positive skin test, which usually may be obtained in the course of six to eight weeks. A small scar results at the site of the inoculation.

At present it may be stated that the organism, cultured, prepared, and injected with rigid care, will probably neither produce tuberculous disease in children nor increase the mortality from tuberculosis in their later life. It is at least as safe as are the living conditions of small children in tuberculous homes, and these are the most proper subjects for its clinical usage. As to the protection conferred to the child, incontrovertible statistical proofs cannot be definitely drawn from any work thus far reported. The difficulties in controlling such work are enormous. The most valuable study at present is that developing in New York City[9], where some 300 children, most of them from tuberculous surroundings, have been parenterally vaccinated. In this study, and in that reported by Wallgren[10] from Gothenburg, we do have evidences of some degree of protection conferred on inoculated children. The differences in both studies have been roughly the same—no tuberculous mortality in the inoculated as against about 3 per cent in the controls. Both studies have, thus far, indicated the safety of the method.

Doubts as to the ultimate wisdom of inoculating any child with a living organism, however attenuated, have led to the work of Petroff, Branch, and others[11], on the use of killed organisms as immunizing agents. These investigators have shown in a series of papers that it is possible by the proper administration of bacilli killed by heat (particularly those of the virulent S strain), to produce not only tuberculin sensitivity but also a degree of immunity. The report of Soper, given above, illustrates experimentally the immunizing effect of this material. Clinically, there should be no doubt of the safety of such inoculation. It is now being used in a study at the Harriet Lane Home in Baltimore[12], where to date about eighty infants have been inoculated. The present dosage is 0.3 mg. injected intramuscularly. This study has not reached the point where its results may be evaluated.

The following conclusions on the general subject of immunization against tuberculosis in childhood seem justifiable:

1. In spite of the drop in mortality there is still a large proportion of deaths from tuberculosis in infants and small children. At these ages, family contact and the persisting use of infected milk are of great importance.

2. It is probable that the non-infected state of these children at the time of their rather massive exposures is a cause of their lack of resistance to the disease.

3. Two methods for the production of relative immunity in infants and children are now available. These substances have been shown to produce a relative immunity in animal experimentation. One of them is attended by the dangers inherent in the inoculation of living bacilli. The other consists of killed organisms. Careful clinical trials of these methods are at present under way in this country. Judgment as to their more widespread usage should be reserved pending the results of these investigations.

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DISCUSSION

CHAIRMAN COBB: The discussion is to be opened by Dr. Eliot H. Luther, of Westfield.

DR. ELIOT H. LUTHER: *Mr. Chairman*—I really find myself in agreement with most of what Dr. Smith has said. I have enjoyed his paper very much, and I find it a little bit hard to take issue with him on most of it. I understand the discusser is supposed to disagree with the writer of the paper if he can, and there are one or two points that I would like to bring out.

In the first place, I do not think you can apply the work on laboratory animals too closely to human beings. In that connection the point that he made, that immunity was probably not related to age but was rather a question of massive infection, plus the absence or presence of allergy, I think the curve of incidence of tuberculosis in the population is rather against. It is true that in infancy, where the disease incidence is quite high, there is also relatively little allergy. So far that would appear to bear out the contention. On the other hand, there is a rather striking drop after the first two years of life, in fact, a very striking drop, and then the disease persists at a very low level indeed until the teens are reached. Now during that time there

is a rising curve of allergy; consequently, a child in the teens should be better protected than the child of seven or eight because there is a higher percentage of allergy present.

Therefore, one would expect the incidence of the disease to continue to decline as the incidence of allergy rose. As a matter of fact, it does quite the reverse. The disease starts to become increasingly prevalent in the late teens and reaches its peak between the ages of thirty and forty. The highest mortality is somewhere in that neighborhood. At that age in the big cities the majority of the population is allergical.

I bring that point out not simply for the sake of disagreeing with Dr. Smith, but because I think it has some bearing on the effect of vaccination against tuberculosis. I think I would agree with him entirely that, if a safe method of vaccination could be found, which would cut down the mortality during the first two years of life, there can be no doubt but that it would be highly desirable. On the other hand, we gain very little by diminishing the mortality in the first two or three years of life at the expense of increased mortality later on. That means that the whole question of allergy and resistance in the human being is very important. If allergy really does increase resistance throughout life, it would be a desirable thing to establish; on the other hand, if it diminishes resistance to the disease in later life, it is highly undesirable and ought not to be established.

I realize that there are no definite figures to show that the allergy produced by vaccination will persist for twenty-five or thirty years.

DR. SMITH: It does not.

DR. LUTHER: It is quite possible that it will not; but there are some interesting observations that seem to show that allergy is detrimental to the individual in later life. In the first place, depending upon the method you use, you can usually demonstrate a preëxisting tuberculous infection in anywhere from 50 to 92 per cent of adults who have later developed pulmonary tuberculosis. In other words, it would seem that allergy is a necessary preceding step to the development of pulmonary tuberculosis in later life.

Rinehart has recently made a survey for the Massachusetts Department of Public Health of the cases which have been seen in the Chadwick Clinic and followed over a period of from seven to nine years, that is, beginning with 1924 and carrying it through to the present time. He found that the incidence of pulmonary tuberculosis in children who had a positive tuberculin test and a calcified lesion by x-ray was 3½ per cent over that period of time. He states that that is thirty-five times the incidence of tuberculosis in the general population at that age. I question his figures a little because his 3½ per cent represents a group that he has followed over a period of seven years on the average, whereas the 0.1 per cent for the general population represents the amount of tuberculosis which would be found if a group of school children were routinely x-rayed, and makes no allowance for the additional cases which would appear if the group were followed for a seven-year period. So, in some ways that comparison is unfair.

On the other hand, he also followed a group of children who were allergical but showed no evidence of tuberculosis by x-ray. He found the incidence there to be 0.7 per cent, and that is certainly no less than that of the general population. He states it is considerably higher. Again his figures are open to the same criticism as the preceding.

At any rate, from these figures I fail to see any evidence that allergy is helpful to the individual, and there is more than a strong suspicion that allergy is harmful. If that is the case, it will take some years before we can decide whether B.C.G. is a safe method of vaccination; and I would quite agree with Dr. Smith that the two or three people who are really doing good work, as is Dr. Parks in New York City, should keep this method of control of tuberculosis in their hands until these questions can be taken out of the realm of opinion and put into the realm of fact.

CHAIRMAN COBB: The second person to discuss this paper is Dr. Arnold Branch of Boston.

DR. BRANCH: *Mr. Chairman*—I shall attempt to give the point of view of the laboratory student of tuberculosis and shall be well content to leave the final decision as to the advisability of vaccinating children against tuberculosis to the clinicians.

As Dr. Smith has pointed out, the object of vaccinating infants is to attempt to lessen the high mortality that occurs from the primary infection. From experimental work on animals we have evidence that primary tuberculosis is entirely different from adult tuberculosis and represents infection of an unimmunized animal or human being; so that for the time being I will limit my discussion to the preventive vaccination against first infection and later return to Dr. Luther's remarks on allergy. The problem of adult tuberculosis is a different one and does not concern us here directly. Dr. Smith has stated that there are only two kinds of vaccine out of the many advocated which are now receiving serious consideration, the use of living virulent organisms and vaccines made from acid-fast organisms other than tubercle bacilli having been pretty well discarded. So we are left with the choice of using avirulent organisms or dead organisms. In either case, the parenteral administration would appear superior to the oral. Of the living avirulent organisms, the strain of Calmette and Guérin (B.C.G.) is the one now most frequently employed because it is controlled by a definite laboratory method, namely culture on potato bile. Of the dead organisms, the method of killing by heat is commonly used. Various other methods of killing have been tried, e.g., chemicals, sunlight, ageing, etc. —too numerous to mention here. I frankly do not think we have yet found the ideal way of killing tubercle bacillus for obtaining the most efficacious antigen, but I have faith that we will ultimately find some way of killing the organisms and producing a dead vaccine which will be equally as effective as an avirulent living one.

To return, then, to the two different methods, that is, the use of avirulent organisms and of dead organisms, let us say a few words about the former as exemplified by B.C.G.

First—is it a good immunizing agent? I think the answer is definitely, "Yes". It is extremely difficult to adduce proof of this in children to-day because too much reliance has been placed on a proved faulty statistical method and many results vitiated by poor controls. In so far as children are concerned, then, I think we have to watch carefully the results of the work that is being done in this country. But certainly in cattle, even if not so much in guinea pigs and monkeys, the bulk of evidence shows that it is a very good immunizing agent.

And secondly, there is the question of the innocuousness of the organism. That interested me when it first came out, and I notice in a rather cursory survey of the literature recently that we still find an occasional instance in which individual strains received from certain laboratories seem to contain virulent forms. Dr. Aronson wrote me recently that

he had received a strain from a well-known laboratory in this country and he had found some virulent forms in it. The avirulence should be constantly controlled where living organisms are used. One practical point comes to mind from what a competent English bacteriologist told me last year. He experienced great difficulty in obtaining any growth from a B.C.G. vaccine he had received from the Pasteur Institute; presumably some of the organisms, only, remained alive. If dead organisms are to be used, surely dead virulent forms would be better than avirulent ones. In order to ensure the majority of bacilli in a B.C.G. vaccine being alive, facilities should be available to guarantee young actively growing organisms as a source of vaccine and rapid distribution and prompt administration.

The more I work with dead organisms of one kind or another, the more interested I become in their possibilities. The recent work of Seibert who has shown that you destroy the antigenic property of tuberculin by heating it above 70°C. is very interesting and it may well be that if organisms killed at 65° were used instead of organisms which have been boiled, better results would be obtained. There are also other methods of killing tubercle bacilli which have not yet been tried.

I would like to read the general opinion regarding B.C.G. vaccination in England and Germany.

A. From the *Lancet*, March, 1933:

1. Tuberculosis mortality in young children is decreasing steadily in Great Britain, and this decrease has been caused exclusively by measures of hygiene, isolation of contagious patients and improved social conditions.

2. It is difficult and often impossible, to separate vaccinated babies from their contaminated families, although this is the essential condition of success in B.C.G. vaccination.

3. It is not yet established how long a child vaccinated with the B.C.G. may resist subsequent virulent infection.

4. It is feared that the introduction of B.C.G. would impair the efficiency of the usual measures of prophylaxis in which the government and local authorities have the greatest trust.

B. From a paper by Nohlen (*Zentr. f. d. ges. Tuberc.*, January, 1932):

Considering the Luebeck fatalities and the unclarified and disputed points, the writer does not believe it opportune to propagate B.C.G. vaccination in Germany. As shown by statistics, tuberculosis in Germany is continuously decreasing. The relative numbers are even below those obtained by Calmette with vaccination. If at all, it should be used only in tuberculous milieu and in specially equipped institutions under strict government control.

I am therefore inclined to think that if we are going to use B.C.G., the ideal way to use it is in carefully controlled experiments conducted by first-class laboratories as is being done in New York and Philadelphia, since very careful handling is needed. One thing I would like to see is a parallel test made with some type of heat-killed or other dead tubercle bacillus.

In conclusion, I should briefly like to touch on Dr. Luther's remarks about allergy. Allergy may be defined as a hyper-reaction to *products* of the tubercle bacillus. It is usually elicited by an intracutaneous inoculation of tuberculin. A positive reaction is merely an index that an individual is hypersensitive to tuberculo-protein and is in no sense an index of immunity, immunity being a resistance of the body to living organisms. The experiments of Rich and his co-workers, I feel, have conclusively shown that it is possible to desensitize tuberculous guinea pigs to tuberculin and still retain their immunity. An allergic animal may be immune, but an immune animal need not be allergic. To summarize my position, I would say that if all the facilities are available, I should be in favor of some form of parenteral vaccination of infants against tuberculosis and should like to see a parallel controlled series run with B.C.G. and dead organisms.

The question of prevention of adult tuberculosis I do not think should be gone into here, because that is a problem in itself.

CHAIRMAN COBB: Those of us who watch the passing of time realize that, with this circle we have here, it is a wise decision to limit the discussions to those people who are familiar with the papers, and if we have time afterwards we will be glad to call on others. So I will ask Dr. Smith if he wishes to make any remarks in closing.

DR. SMITH: *Mr. Chairman*—I think that I have really nothing to say except to thank both discussers for their added points, and to ask that my remarks be not interpreted as a plea for vaccination but simply as a presentation of a subject which I think is somewhat important at present. Otherwise, the material is too vast to try to go into it further at this time.

CHAIRMAN COBB: Dr. Maurice E. Smith, of the Worcester Polytechnic Institute, has been sent to us through the courtesy of Dr. Jennings to tell us a little bit about something we do not know—this bacillus Welchii or bacillus aerogenes capsulatus and its effect in milk, which I think will interest every Fellow in this room.

DR. MAURICE E. SMITH: *Mr. Chairman and Members of the Pediatric Section of the Massachusetts Medical Society*—Dr. North, of Baltimore, in 1933, investigated certain samples of pasteurized milk and found that, after heating the samples for ten minutes at 80 degrees Centigrade followed by incubation at 37°C. for twenty hours, there was considerable gas formation. He claims to have isolated and identified bacillus Welchii as the gas former.

At the Worcester Polytechnic Institute we examine large numbers of samples of milk, both pasteurized and certified, for the Medical Milk Commission, and became interested in this test, and have carried out an investigation into this problem since last fall.

The test is quite an old one, probably twenty-five years old. It was used in the routine testing of milk samples in 1910. Following the English usage for a similar method the test was named the "bacillus enteritidis sporogenes" test.

A large number of investigators have studied this problem and have showed that the term bacillus enteritidis sporogenes covers a large number of species of bacteria ordinarily present in the intestinal tract of animals, and in but few instances has it been possible to isolate the specific organism that causes this gas formation in milk. We have investigated a large number of pasteurized milk samples, and one sample in particular which always gives this gas formation, and conclude that another bacillus than bacillus Welchii is present.

Hammar, of the Iowa State Board of Health, who investigated the same problem in 1923, found this same fermentation to be brought about by bacteria of the bacillus butyricus group.

The bacillus that has caused the gas formation which you observe in the various bottles of milk on exhibition here on the table, gives a gas ratio of 1.2 of hydrogen to 1 of carbon dioxide. It is stated that bacillus Welchii gives a ratio of 2:1 to 3:1. I asked a bacteriologist whether this had any significance and he stated that a bacteriologist never pays any attention to gas ratios. I do not know whether it has any particular significance. The particular bacillus concerned ferments dextrose slowly and lactose very rapidly, and after several days there is a strong odor of butyric acid. Bacillus Welchii and bacillus butyricus both produce the same end products. Examination of the serum showed the presence of gram positive rods and a streptococcus.

On the table before me are a number of agar plates containing nutrient agar with dextrose and lactose. You will note particularly on the lactose-agar plates evidence of fermentation, a large bubble of gas, in which is a colony. The bacteria comprising this colony will not ferment lactose. If you examine the area around the edge of the bubble with a lens you will find a small amount of serum, and this serum when placed in lactose broth will cause fermentation of the sugar and produce butyric acid after three or four days, but we have not been able to isolate any particular bacillus from the serum.

The test devised by Dr. North and described in "Certified Milk" is called a household test. Of course it would be a rather expensive proposition to be tried with certified milk, but not with pasteurized milk. The cap is loosened on the bottle of milk, and the bottle set in a kettle of water at room temperature. The water is heated slowly to a temperature of 80°C., held at that temperature for ten minutes, the cap pressed in, the bottle removed and inverted in a beaker. After eighteen to twenty-four hours at room temperature, if fermenting spore formers are present, there will be a copious gas formation and the curd separates and seems to be punctured with gas holes.

This is one test for Bacillus Welchii, but Kendall states that this bacillus turns the curd pink. We have never observed the formation of a pink curd and we have examined regularly over the past few months one brand of pasteurized milk which ferments in this manner regularly in eighteen to twenty-four hours.

We have investigated a sample of milk powder that is on the market and have found that it contains a similar type of bacteria and ferments readily when treated in this way.

It is possible that the bacteria bringing about this fermentation may be of the thermophilic type. The spores of many of this type will stand a temperature of 100°C. for five to eight hours before being killed. Many of these will ferment sugars.

We have not sufficient evidence at the present time to state definitely that this test indicates manurial pollution. It may be the result of pollution by stable dust or air-borne dust, but indicates that conditions surrounding the handling of pasteurized milk are not so clean as they might be. This test, which is an old one, is a help to determine if milk is as clean as it should be.

I understood in coming here that I might have ten minutes for this address and as there are but three or four minutes left, I would like to devote them to the answering of any questions, that you may care to ask.

CHAIRMAN COBB: Are we to understand that the certified milks give no gas displacement?

PROFESSOR SMITH: Seldom. Occasionally we find a sample that will, but I do not think that it is any evidence of manurial pollution. There are a large number of bacteria present in stables that will bring about this fermentation.

DR. SMITH: I have some photographs of typical fermentations which I will leave here on the table and you may examine them after the meeting. Here is one of a milk sample that was kept at 100 degrees for ten minutes and gave gas formation, showing that the spores were not killed at this temperature in ten minutes.

CHAIRMAN COBB: 100 degrees Centigrade?

DR. SMITH: Yes. All were heated at the temperature noted for the same time and still the spores grew as well after one treatment as after another. This is apparently quite a resistant bacillus.

DR. WALTER L. JENNINGS: *Mr. Chairman*—If I might add one further word with respect to the last subject, the results which we have had demonstrate beyond question the cleanliness of certified milk, whether it be pasteurized or un-pasteurized milk. They have demonstrated also that the market milks as pasteurized do not stand up under the test; in other words, that in the market milk pasteurized, the milk was unclean from my standpoint before it was pasteurized, and there is no means by ordinary plate culture to determine that fact. This test which Dr. North has brought out, as Dr. Smith truly says, is a very old one, but it does give one an easy method of detecting whether the pasteurizer was pasteurizing what we call clean milk. I want that point brought out very clearly, that it shows the value of certified milk as the ordinary producers are making it here near Boston and in Worcester County.

CHAIRMAN COBB: Thank you, Dr. Jennings.

SPEAKER FROM THE FLOOR: May I ask Dr. Jennings a question? Will two-minute boiling help that at all after the milk is pasteurized first?

DR. JENNINGS: No, sir. It will if you boil it long enough, but just ordinary boiling, just a few minutes, will not suffice.

CHAIRMAN COBB: Thank you, Doctor. This is only part of the program that Worcester is providing. I suppose you realize that, and we appreciate it, gentlemen.

CHAIRMAN COBB: Since I have been in practice, many theories as to the cause of sudden death in infancy and childhood have fallen into the wastebasket, or, if we can't find any cause for a sudden death, we apply some such wastebasket theory. For that reason we are very glad to have to-day an article on the rôle of the streptococcus in so-called sudden death in infancy and childhood, by Dr. Sidney Farber, of the Harvard Medical School. Dr. Farber.

FULMINATING STREPTOCOCCUS INFECTIONS IN INFANCY AS A CAUSE OF SUDDEN DEATH*

BY SIDNEY FARBER, M.D.†

INSTANCES of unexplained sudden death in early life occur with sufficient frequency to justify periodic consideration of this problem. It seems worthwhile, therefore, to record some recent experiences with *one* cause of sudden death in early life.

The streptococcus is but one of many organisms capable of causing fulminating infection in early life. Among others which we may mention are the staphylococcus, the pneumococcus, the meningococcus, and the dysentery bacillus. It has been our experience, however, that the streptococcus is the most common and we have been impressed by the large number of infants and children who have died suddenly after an illness of only eighteen to forty-eight hours' duration. The clinical picture may be so bizarre that great difficulty in diagnosis is often encountered. The greatest incidence has been found in the winter months, although such cases have occurred at all seasons of the year. The following story is fairly typical of this group:

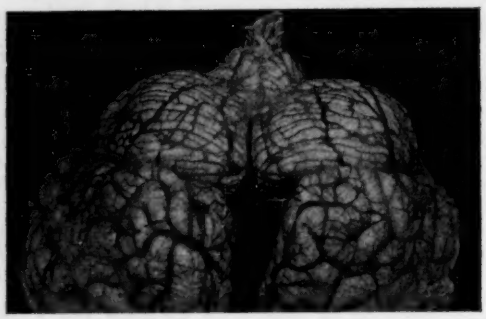

FIG. 1. Photograph of base of brain of child 4 5/12 years of age. Death was caused by fulminating streptococcus bacteremia. Note marked pressure cone caused by herniation of cerebellum into the foramen magnum. Cerebral edema is a constant and important finding in cases of this type.

A child of 2 2/12 years (A-33-16) entered the hospital with a story of convulsions for eight hours. On the day before entry he was said to have been a normal, healthy child, although on the night before entry his sleep was restless. A convulsion at 8:00 o'clock of the morning of entry was his first definite symptom. At 9:00 o'clock he appeared normal and at 10:00 o'clock he had a second convulsion and coma ensued. Six more convulsions occurred before entry to the hospital at 6:00 P.M., ten hours after onset of his symptoms. On physical examination he was a very well-developed boy, lying limp and unconscious in bed. His left knee and arm were flexed and were moving slowly while the right leg and arm were flaccid. His head was turned to the left. The neck was not stiff and the Kernig sign was not present. The white count was 33,000 with 82 per cent polymorphonuclear leucocytes. After admission almost constant generalized convulsions involving mainly the right side of the body were noted. Because of the right-sided nature of the convulsions a neurological consultant suggested a subdural tap on the left side. This was done six hours after entry and no blood was found. The temperature rose to 107° and the patient died at 4:20 in the morning, about ten hours after entry and approximately twenty hours after the onset of his first important symptom.

At autopsy a streptococcus hemolyticus was isolated in pure culture from the blood stream. Early interstitial bronchopneumonia and peribronchitis were found. There was marked, diffuse edema of the brain, optic nerves and spinal cord. No local cerebral lesions were found. The kidneys were enlarged, pale and swollen and on microscopic examination the epithelium lining the tubules showed marked fatty degeneration. Numerous venous thrombi were noted on microscopic examination in the lungs and other organs of the body. "Toxic" changes in the spleen and lymph nodes were also prominent microscopic features.

We have encountered at autopsy a large number of similar cases, where the patient was said to have been perfectly well until the sudden onset of the fatal illness. In others there could be obtained a story of a cold, sore throat, otitis media, or an acute cervical adenitis. The rapid onset, short, severe course, high temperature, neurological manifestations including coma, and other evidences of critical illness, have been the most frequent clinical findings. Pathological changes have been quite uniform. An interstitial bronchopneumonia (the type most often caused by the streptococcus), cerebral edema, and edema of the optic nerves and cord, petechial hemorrhages in the lungs, heart, kidneys and in the liver, microscopic venous thrombi in the lungs and elsewhere, and "toxic" changes in the spleen and lymph nodes are common findings. In a few cases there was found evidence of terminal meningitis, peritonitis, pericarditis, pleuritis and other manifestations of the bacteremia.

The organism may enter by way of the upper respiratory tract, the gastro-intestinal tract, or from an older focus of infection in the body as, for example, an acute cervical adenitis. In most of the cases a streptococcus hemolyticus was isolated from the blood stream at autopsy and in many of the cases this finding was made during life. In a smaller number no growth was obtained from the blood stream although gross and histological changes in these cases were identical with those in which a positive culture was found.

The disease described is not primarily a pneumonic process; it is rather a widespread in-

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From the Department of Pathology, Harvard Medical School and the Pathology Laboratory of the Boston Children's Hospital.

†Farber, Sidney — Pathologist, Boston Children's Hospital, Boston. For record and address of author see "This Week's Issue," page 187.

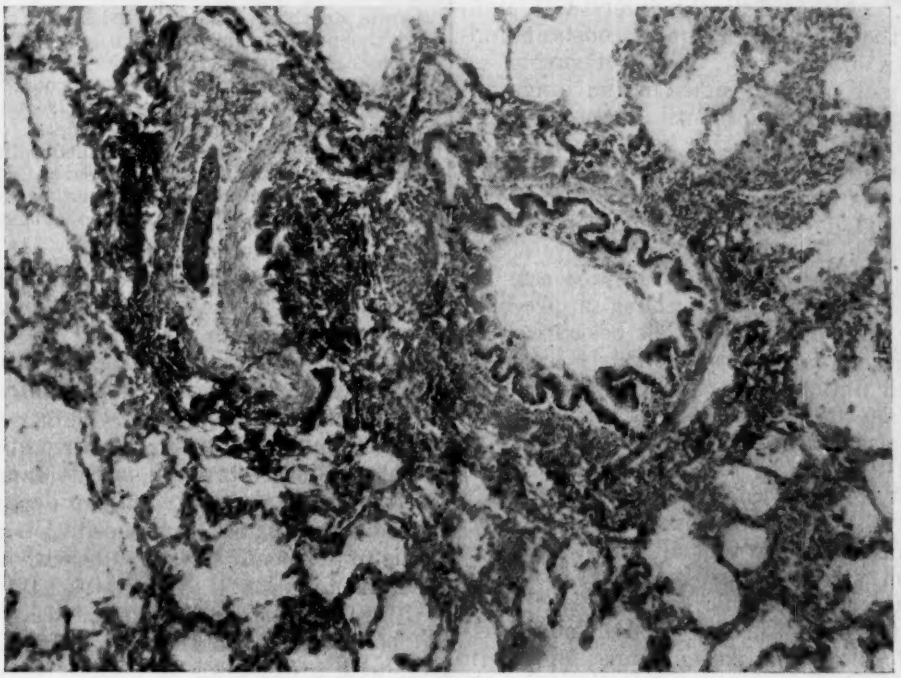

FIG. 2. Photomicrograph of lung of child, age 2 2/12 years, who died twenty hours after the sudden onset of convulsions. Death was caused by a streptococcus bacteremia. Note recent thrombus in a small vein, slight peribronchitis and thickening of alveolar walls. The alveolar spaces contain no exudate. Hematoxylin and Eosin × 75.

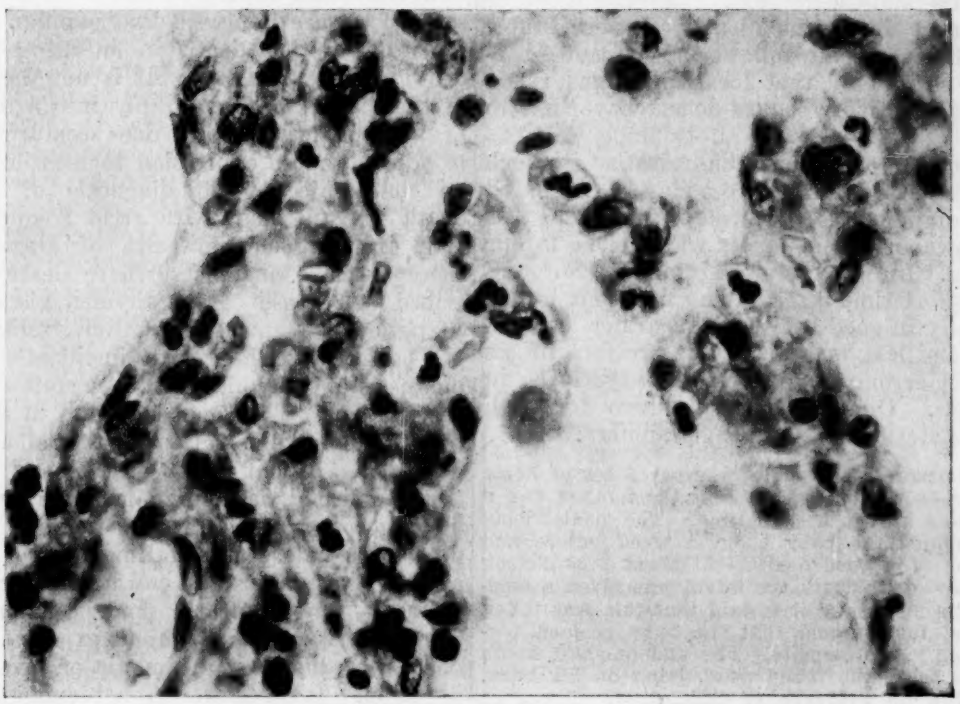

FIG. 3. Photomicrograph of lung showing higher magnification of thickened alveolar walls seen in fig. 2. Note that thickening is due to the infiltration of the alveolar walls by polymorphonuclear leucocytes and large mononuclear cells. Hematoxylin and Eosin × 780.

volvement of the entire body secondary to a bacteremia. Although early interstitial infiltration of the lungs is an almost constant finding in cases of this type, it is not surprising that abnormal physical signs in the lungs are usually absent. It is not until severe injury to the alveolar wall capillaries has occurred with resultant exudation of fluid and cellular elements into the alveolar spaces and bronchioles, that râles and dependable evidence of dullness can be elicited. Death, however, usually occurs in most cases of fulminating streptococcus infections before an important or appreciable amount of lung parenchyma has been involved.

We believe that with the fairly constant pathological findings associated with a finding of the streptococcus hemolyticus by blood culture in the majority of cases, a fairly definite disease picture can be recognized. It must be emphasized that this picture is but one of the variations of streptococcus infections in early life. We do not imply that all individuals who suffer from streptococcus infections follow a fatal course. Considerable variation in the virulence of the organism and in the immunological reactions of the patient must obtain to account for the numerous gradations in the severity of the clinical course and the degree of involvement of the body. We are all acquainted with other manifestations of streptococcus infection in early life, such as acute and chronic bronchopneumonia, pharyngitis, retropharyngeal cellulitis, descending tracheobronchitis, omphalitis and meningitis. The instances of fulminating infections described here differ mainly because death follows the onset of a bacteremia so quickly that localizing signs referable to one or more organs do not have time to appear.

The streptococcus may cause death with such rapidity that its killing effect may be compared to that of powerful chemical poison. This was well shown in two instances which came to our attention. In both cases the infants were found dead a short time after having been put to bed apparently in good health. The strange circumstances and lack of a history of previous illness led to an erroneous diagnosis of *suffocation* in each case. One history will serve for both since the stories were strikingly similar:*

A three months' old baby was cared for at home by a nurse due to the fact that the mother had a severe sore throat at the time. The pediatrician had examined the baby about a week before and had found it in good health. At about 2:00 o'clock on the day of its death the infant was given a feeding by the nurse and it is said that this was taken in normal fashion and that the baby seemed perfectly well. Approximately one and one-half hours later the baby was found dead, lying on his back. There was no evidence of bedclothes, pillow, or any other object over his face. The fire department was called and an apparatus for resuscitation (probably the Henderson and Haggard apparatus) was used, without success. The body was released with a diagnosis of "suffocation" and an autopsy was requested by the pediatrician. The diagnosis of "thymic death" was also considered.

At the postmortem examination a pure culture of streptococcus hemolyticus was isolated from the heart's blood. In addition streptococci were grown from the lung and were seen in direct smear made from the thin, seropurulent exudate found in the bronchi. There was edema of the brain and spinal cord. Microscopically a very early interstitial infiltration of the alveolar walls and peribronchial regions was found. There was no evidence of suffocation.

*Dr. Robert Curtis, Boston, kindly supplied the clinical data.

The findings in this case are similar bacteriologically and pathologically, although to a less marked degree, to the cases of fulminating streptococcus infection where death occurred after a clinical course of from eighteen to forty-eight hours.

We would like to emphasize two additional points of interest which were common to both cases of sudden death: the fire department was called upon for aid in resuscitation and a diagnosis of *suffocation* was made without postmortem examination.

Since a number of similar cases were said to have occurred in Massachusetts this past winter, with a diagnosis of either "thymic death" or "suffocation", it may be of interest to discuss briefly some of the common explanations for sudden and unexpected death in early life. If we exclude such obvious causes of sudden death as trauma associated with falls or automobile accidents, or suffocation following aspiration of foreign bodies, or carbon monoxide poisoning, we are left with two popular explanations of sudden death in infancy: "thymic death" and *suffocation*. It is not the purpose of this paper to enter deeply into a discussion of "thymic death" but it does seem worth while to add one more expression to recorded feeling on the subject. The diagnosis of "thymic death" is still made with great frequency. In 1932 in the Commonwealth of Massachusetts there were 76 instances where death was ascribed to disease of the thymus gland (Vital Statistics of Massachusetts, 1932, table 14:67). We believe that there is no justification for the diagnosis of "thymic death" or status thymicolymphaticus. There can be found in the literature numerous illustrations of the fallacy of this diagnosis. About twenty-five years ago Dr. S. B. Wolbach[1] was able to demonstrate an early meningococcus meningitis in a child who had died immediately after falling from a swing in a West-End playground and upon whom a diagnosis of "thymic death" had been made. We recently have had a similar experience where death was due to a pneumonia of several days' duration. It is, however, not enough to give negative evidence on this important subject. Such examples point merely to the fact that an error in diagnosis has been made. It is of interest in this connection to note that the diag-

nosis of "thymic death" is very often made without benefit of postmortem examination. In those instances, however, where such a diagnosis is made after autopsy, it is based upon the popular misconception of the size of a normal thymus. Due mainly to the exhaustive work of Hammar[2] in Upsala and Boyd[3] in Minnesota, pathologists are now equipped with a precise standard for evaluating the weight of the thymus, and with a clear idea of the amount of lymphoid tissue present in the body of a normal, healthy and well-nourished child. They have shown that what was formerly regarded as a normal thymus, represents really a pathologically involuted organ.

In the last 2000 consecutive autopsies at the Boston Children's Hospital we have been unable to find a thymus which we could regard as pathological in size, nor have we found in any case a thymus which has been associated with definite symptoms during the life of the patient. During the past five years we have been able to collect a series of ten instances in which the weight of the thymus lay between forty-five and sixty-five grams. In these cases no symptoms referable to the thymic region were noted during life and in every case an adequate cause for death, not associated with the thymus, was found. The great harm in making what we regard a fallacious diagnosis of "thymic death," lies mainly in the fact that further inquiry is halted. Such a diagnosis provides an easy way out in distressing incidents of sudden death. That, however, is no excuse for the maintenance of a belief which was born in a period of misinformation and which has been fostered by inadequate observations to the present time.

The second diagnosis which is commonly made in cases of sudden death in early life is *suffocation.* In 1932 in the Commonwealth of Massachusetts there were forty-eight deaths due to accidental mechanical suffocation (Vital Statistics of Massachusetts, 1932, table 14: 182). It is interesting to note also that in the United States Birth Registration area for 1929 approximately 35 per cent of all deaths from external causes, during the first year of life, were recorded as due to suffocation, although that diagnosis does not appear with sufficient frequency in the age groups after the first year to warrant a place upon the prepared charts[4]. The diagnosis of suffocation in the two cases of sudden death about which I have spoken was made without postmortem examination. This diagnosis has been in part an outgrowth of the accident termed "overlying" and is therefore graced with historical dignity. We find in the "Judgment of Solomon" I Kings iii:XIX, in the famous trial where two mothers claimed the same baby, the following evidence: "and this woman's child died in the night because she overlaid it." Cases of true overlying or suffocation from that cause undoubtedly occurred in past years when a heavy mother slept in bed with several children and the new-born baby. The conditions, however, are quite different when a baby is found dead in its own bed or crib, without any evidence of foul play or of accident. In the two cases which I have cited where the diagnosis of suffocation had been made, postmortem examination *happened* to show evidences of streptococcus bacteremia. It seems fair to assume that if careful examinations were carried out in other instances of "suffocation" an adequate cause for death, other than suffocation, might be found. At any rate it seems logical to suggest that such a diagnosis should not be made merely upon the basis of a story of sudden unexpected death and observations on the outside of the body. It is beyond my province to do more than mention the unfortunate social and family aspects of a situation following the sudden death of a baby with diagnosis of suffocation and the implication that death was caused by negligence on the part of the parents. The irony of the situation is apparent in the two instances I have described, in view of the fact that the diagnosis of suffocation was not borne out by more careful study.

It seems reasonable to assume that the history in cases of sudden death due to streptococcus bacteremia may not be entirely accurate. Such cases of sudden death are associated with so much shock to the family that an accurate history is impossible to obtain. In one of the cases of sudden death cited here a history of "snuffles" of two days' duration was later obtained and this probably provided the starting point of the bacteremia which caused death so unexpectedly.

SUMMARY AND CONCLUSIONS: The streptococcus hemolyticus is a common cause of fulminating infections in early life. Death may occur within eighteen to forty-eight hours after onset of symptoms. The clinical signs may be bizarre in character and diagnosis may be difficult. Convulsions, coma, extremely high temperatures and other signs of critical illness are present. The most important findings at autopsy are edema of the brain, spinal cord and optic nerves, early interstitial bronchopneumonia and evidences of damage, secondary to the bacteremia, in the kidneys, liver, spleen and lymph nodes. Findings similar to these, but to a less marked degree, were made in two cases of sudden death in infancy where a diagnosis of suffocation had been made without postmortem examination. It is suggested that the history in cases of sudden death may not be entirely accurate. These two cases of sudden death illustrate the extreme rapidity with which the streptococcus may cause death. It may be emphasized that we have described but *one* of the causes of sudden death in early life, and do not

imply that all cases of sudden death can be explained in the same way. We believe that there is no justification for the diagnosis of "thymic death". The diagnosis of suffocation in early life when factors such as carbon monoxide poisoning and foreign bodies can be ruled out should not be accepted unless a complete postmortem examination is performed.

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4 Charts prepared by Dr. Harold C. Stuart, Harvard School of Public Health, to whom thanks are due for the use of his data.

DISCUSSION

CHAIRMAN COBB: This paper is to be discussed by Dr. Richard M. Smith, of Boston.

DR. RICHARD M. SMITH: *Mr. Chairman*—Dr. Farber has really given us two papers, and I want to say something about both of the matters which he has presented. First of all, with reference to sudden death which is dependent upon streptococcus infection. As Dr. Farber has said, all of us are familiar with manifestations of streptococcus septicemia, but I think that until recently we have not appreciated the suddenness with which death may be caused by this condition. We have been unfortunate in having seen at the hospital a considerable number of these children within recent years, especially within the last twelve months. The lesson we should learn from this part of the paper which Dr. Farber has presented is to be constantly on our guard to remember that this condition may be present in children who are taken seriously and suddenly ill. A considerable number of them who present on examination almost no physical signs of localized disease die very promptly and will be found at autopsy to have had an overwhelming streptococcus septicemia.

The postmortem finding of lesions in the lungs, sometimes in very early stages and sometimes in a more advanced form, is interesting because we are always looking for possible early pneumonia in these patients. After having seen Dr. Farber's slides we can understand why the physical examination is entirely negative, although the disease may be so advanced as to cause death.

The other thing I want to mention is the question of making the diagnosis of "thymic death". We, as physicians, are very much to blame for the apprehension which is so prevalent among the laity of the danger of sudden death in children from enlarged thymus. We have perhaps been unwilling to stand up in our boots and say we do not believe that an enlarged thymus is a cause of death. It is, as Dr. Farber said, an easy escape for us when a sudden death occurs which we cannot adequately explain.

It is a common procedure to take an x-ray of all newborn babies with a view to discovering a possible enlarged thymus and giving an x-ray treatment to decrease the size of the thymus with the expectation that sudden death may be prevented. As we know, the technique which is usually adopted is to take a single flat plate. This gives us no accurate information with reference to the size of the thymus because the size varies considerably during the twenty-four hours, even during the process of respiration, and a single flat plate does not help us at all to determine whether the thymus is enlarged. And even if it were enlarged, which might be determined by accurate observation, there is no conclusive evidence that it does any particular harm. Children who have been shown to have a shadow larger than that cast by a supposedly normal thymus, if not treated, do exactly as well in a large proportion of cases as those that have been treated. So that we have no real evidence that the roentgenogram helps at all, or that the method of treatment adopted is of any value, and we have a good deal of evidence that the pictures are of no value, and that the treatment does not do any good.

It seems to me, therefore, that we have arrived at the point where we ought to be willing to combat the popular demand for the taking of an x-ray flat plate of every newborn child, hoping that we shall by that means detect a possible enlargement of the thymus and by treatment prevent death.

Another occasion when the thymus is investigated is before surgical operations. It is a very convenient method of explaining sudden death during operation to say that the patient probably had an enlarged thymus. I recall that Dr. Frank Richardson told me but a short time before he died that in his experience he had never known a death due to a large thymus, that every death which occurred during anesthesia could be explained on some other basis. I think we ought to take a stand on this matter also and recognize that most of the evidence upon which the diagnosis of enlarged thymus has been made is bad, and that the cases of sudden death, if properly investigated, will prove to have some other explanation for the death rather than enlarged thymus.

I believe that we ought to be as aggressive in our attitude, as much so as we have been in the past in talking about the dangers of an enlarged thymus, because as the result of our previous discussion we have created a fear in the lay mind which is entirely unjustified and which we have a real responsibility to alleviate.

CHAIRMAN COBB: The next discusser is Dr. Karlton G. Percy, of Boston.

DR. KARLTON G. PERCY: *Mr. Chairman and Dr. Farber*—Often we hear at medical meetings a paper which is scientific and applies only to medical aspects. This is a paper that opens a wide field, not only medical but of vital importance from the social point of view.

I happen to know two of the parents of the children whose sudden deaths were reported here, and Dr. Farber did not tell you the little story that went with the second. They both happened to be patients of one doctor. After he had demanded the autopsy on the first infant that died so suddenly which proved that death was caused by a hemolytic streptococcus infection, his mind reverted to the other child that had died some three or four weeks before.

The diagnosis, on this infant of suffocation, was made by the medical examiner. At the time of death the mother happened to be downstairs playing bridge with a neighbor. It was her only child and her first child. After the death of her infant she had fallen into a mental depressive collapse and sanatorium treatment was being planned for her. Her doctor hoped they could help by exhuming the body and making an autopsy. The body was exhumed. The autopsy was made. Of course the organism was not found in a live culture but it was found in the brain microscopically. The diagnosis of a streptococcus infection death was made and the stigma of maternal carelessness vanished. Almost miraculously she recovered her mental poise,

knowing that the child died with an acute infection rather than from suffocation.

Now that is happening everywhere. And so it is up to us, as physicians, after a paper of this sort has been read, to do everything possible to procure an accurate diagnosis on sudden deaths and avert the phobia which we, as medical men, have allowed to rise in the mind of the layman.

It was only the other evening that a lay discussion arose before a medical man. The grown child of a doctor had died suddenly—"thymic death". A cousin of the parent had also lost a child by sudden death, diagnosed also thymic death, and the question arose as to whether there was anything familial and whether those individual parents should have any more children.

The cause of it all was the phobia which the medical profession had previously aroused.

Furthermore, if a child dies and a diagnosis of thymic death is made, there is not only the unhappiness to the parents, but there is the stigma which is put upon the medical man, who has taken care of that child, that he has not previously made a diagnosis of thymus and not had the child treated. If thereby we can help by seeing to it that all the children who have sudden deaths are examined, we are going to put the world socially into a better frame of mind in regard to one of the unpleasant end results in infancy.

There is no doubt, after the autopsy, that these two deaths were from streptococcus. It is too small a series to accept as a final cause of all sudden medical deaths in infants. I happen to have seen one of these autopsies, seen the slides and the pathologic sections and there is no doubt as to the cause of death. Let me go on further and prove that no sudden deaths can be ascribed to the thymus.

Now let us go back to the question of the thymus medically. We have been brought up with the idea that the thymus can do all and sundry things. In the old days it was a bugbear and one of the worst bugbears, and, as Dr. Smith has brought up, there have been institutions that have always taken plates of every newborn child. The economic cost has been tremendous. However, although I was brought up in that school, I have felt from my own observations that there is such a thing as an enlarged thymus which produces symptoms. After a thymus has been found enlarged by x-ray, I have promptly gone ahead and had the x-ray treatment given. In my own mind I have felt a whole lot easier in having this done.

Around 1910 there was the belief that the thymus could produce all of these awful symptoms and tragedies. From 1920 on there has been the belief that there is no such thing as any symptom coming from the enlargement of a thymus. I am going to take the middle course. I have never yet seen a proved thymic death. Yet should a patient show symptoms which are referable to the thymus, should an x-ray uphold this belief that the thymus is enlarged; should the x-ray therapy which is done, not only diminish the shadow of that thymus but relieve the patient of symptoms and the family of this fear—then, until it is proved that the thymus is absolutely an innocent organ, I feel that we, medically, are justified in taking the necessary steps to have it treated by x-ray.

Lastly, let us give Dr. Farber and our pathologists every bit of assistance possible, in proving that there is no such thing as a thymic death.

CHAIRMAN COBB: Dr. Farber, will you please close?

DR. FARBER: I have nothing further to add.

CHAIRMAN COBB: Before I ask for the last paper, I will say that the committee I appointed happened to be sitting close together. I did not know it at the time. They have nominated for the ensuing year Dr. Joseph Garland of Boston as Chairman and Dr. James M. Baty of Boston as Secretary. Has anyone any suggestion of any other nominations? If not, we will ask all those in favor of these nominees to say Aye, those opposed No, and I declare them elected for the coming year.

CHAIRMAN COBB: The last paper which we have is the paper entitled "Pyogenic Infection of Bones and Joints in Infants", by Dr. William T. Green, Children's Hospital, Boston.

PYOGENIC INFECTIONS OF BONES AND JOINTS IN INFANCY*

BY WILLIAM T. GREEN, M.D.†

PERHAPS it would have been better to have entitled this paper "The Problem of a Sick Infant with a Painful Extremity." It is so much our tendency to concentrate upon the head and trunk, particularly the respiratory and gastro-intestinal symptoms, as the possible site of origin of an acute illness that we are rather prone to neglect the consideration of lesions in the extremities.

Unfortunately, an infant cannot tell us where pain is located; we are forced to depend primarily upon objective findings. The mother may notice that an extremity is sensitive, but frequently she may not. It is particularly necessary that in all instances of an acute illness the physician should examine the extremities even if a possible cause for the illness is found elsewhere, as for example, a respiratory infection. As we have pointed out in a previous communication, approximately 60 per cent of all cases of osteomyelitis in infancy showed antecedent or concomitant infections elsewhere, the majority of which were respiratory. It is thus quite easy to pay entire attention in a sick infant, to an acute tonsillitis which is subsiding, whereas the real cause of the present acute illness is a septic joint or an osteomyelitis. Both of these conditions are relatively common in infancy. Septic joint is more common in infancy than at any other time; whereas osteomyelitis is as common then as at any age period.

One should, then, in any acute illness, examine the extremities for the presence of pro-

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†Green, William T. — Junior Assistant Orthopedic Surgeon, Children's Hospital, Boston, and Peter Bent Brigham Hospital, Boston. For record and address of author see "This Week's Issue," page 187.

tective muscle spasm on motion, tenderness to palpation, and swelling. This examination may be very rapid and relatively brief, but it may save considerable embarrassment.

If the examiner finds in a sick infant with an otherwise unexplained acute illness—tenderness, muscle spasm or swelling in the extremity, what then? How shall he arrive at the diagnosis? Is it essential to make an immediate diagnosis? Does the immediate therapy depend upon an immediate diagnosis? Once the diagnosis is determined, what shall the treatment be for the particular lesion? For example, if it is osteomyelitis, is an immediate operative procedure essential? Is the prognosis affected by delay? It is in an attempt to answer these and similar questions that I should like to present and discuss three representative cases.

CASE I. L. F., aged nine months, was brought to the hospital with a complaint of an acute illness of eight days' duration associated with pain in the region of the left knee. The child's health had been excellent previously. At the onset of the acute illness the mother noticed that the child cried when the left knee was touched but nothing unusual was noted about the knee except for this. The day after the onset the child was seen by her physician, who advised hot compresses. The following day the knee began to swell and was very painful; accordingly a liniment and massage were prescribed for the "rheumatism" of the knee. The child had slept very poorly and apparently had been in great pain throughout the period.

Examination showed a well-developed, acutely but not severely ill infant whose general physical examination was not particularly noteworthy except for examination of the left lower extremity. The entire thigh, knee and upper portion of the leg were swollen, shiny and tense with increased local heat. The knee was held in ninety degrees flexion by marked muscle spasm. All attempted motions of the joint were very painful. The tenderness was most marked over the synovia, and the joint capsule was definitely distended and fluctuant. The temperature was 103 degrees. The WBC was 23,000. *The roentgenogram was negative* except for swelling of the soft tissues. A diagnosis of septic knee (or pyarthrosis) was made.

Accordingly, on the day of admission the knee was drained by two longitudinal incisions on either side of the patella. The joint capsule was markedly distended with relatively thick purulent material which on culture showed pneumococcus. The knee was thoroughly lavaged with a normal saline solution for ten minutes and the knee joint was marsupialized by sewing the synovia to the subcutaneous tissue. Postoperative care was essentially that of infrequent dressings and immobilization by traction in a Thomas splint with gradually increasing periods of freedom from the splint after the fifth day. The child was discharged one month after the operation with both wounds healed. For home use a plaster cast was given which was to be applied at night to maintain extension of the knee. At the last examination, six months following, motions of the knee were completely normal.

DISCUSSION OF CASE I; DISCUSSION OF DIFFERENTIAL DIAGNOSIS IN SEPTIC JOINT

This child gave a rather typical history of a septic knee, although frequently the illness is more fulminant in character. Evidences of severe pain are usually presented very early; in fact, severe pain, flexion-deformity and marked muscle spasm on any attempted handling are typical of septic joints throughout their course. In no other acute lesion is there so much muscle spasm and resistance to motion. Many times, if the child is seen within a few hours after the onset, one may detect marked muscle spasm and extreme sensitivity on attempted motion of the involved joint which is held in flexion deformity, with palpation revealing fluid in the joint. On the basis of these findings alone in an acutely ill infant without any other obvious cause for the illness, a tentative diagnosis of septic joint may be made. One should like to have these findings associated with an elevated white blood count.

If the illness is of several days' duration, the presence of fluid in a joint provoked by an adjacent osteomyelitis without the joint itself being involved may be confusing. Usually in these joints, the amount of fluid is less than one would expect in a septic joint of similar duration, there is less muscle spasm and pain on motion if the movement is carried out carefully, and the maximal tenderness is not over the joint but over the metaphysis. However, the determination of the site of maximal tenderness is frequently unreliable in an infant. Thickening over the bone in osteomyelitis may be palpated but frequently the swelling is so diffuse that this determination is of little aid. In this patient, for example, the entire thigh was swollen as was the proximal half of the leg although only the joint was involved. Infants show a widespread diffuse swelling of the extremity whether the lesion is a septic joint, osteomyelitis, or a cellulitis. Usually a septic joint shows less diffuse swelling than do the other conditions.

One may, if unable to be sure of the diagnosis in the presence of fluid in a joint, aspirate some of the fluid for examination. However, one should not indiscriminately "plow" into a joint with subsequent injury to the cartilage. Usually aspiration is unnecessary to make the diagnosis.

Of the possibilities to consider in differential diagnosis besides osteomyelitis and cellulitis which are the most confusing, tuberculosis must be mentioned though little confusion is possible. Tuberculosis of large joints is extremely rare under two years of age, and if it is present should be easily differentiated. Likewise, rheumatic fever at this age need not be considered. Proliferate arthritis does occur in infancy and the examination of the joint alone might possibly give rise to some perplexity, but the slow onset, the involvement of multiple joints, the general clinical picture, and the less sensitive joints of arthritis make the differentiation sim-

ple. Scurvy with infection elsewhere usually is not confused with a septic joint but may be confused with osteomyelitis. Likewise congenital lues might give rise to some perplexity. The absence of local swelling and the general clinical picture should serve to differentiate early infantile paralysis. Furthermore, as septic joints secondary to osteomyelitis are more common in infants than in older children, this possibility must always be considered.

Roentgenograms should be taken, but usually in the early stages they are of little aid in the diagnosis. However, roentgenographic evidences of osteomyelitis are seen earlier in infants than in older children, and one may obtain an idea of the distention of the capsule in a septic joint. Likewise such conditions as scurvy and congenital lues may be recognized.

In general, a septic joint is one of the easiest lesions of the extremity to recognize except in the case of the hip joint; often it is almost impossible to differentiate a septic hip from an osteomyelitis of the neck of the femur.

TREATMENT AND PROGNOSIS IN SEPTIC JOINT

Once the diagnosis of septic joint is made, the treatment is essentially that of early adequate drainage. If there is doubt about the diagnosis or if the general condition of the patient contraindicates operation, delay in carrying out the operative procedure is desirable. Needless to say, since normal motion in addition to a recovery from the acute illness is desired, proper after-care is just as important as the operation. However the discussion of details of therapy is not in the province of this paper.

We are thankful that the prognosis, so far as the function of the joint is concerned, is better in infancy than in the older individuals. This is probably due to the thicker cartilaginous plate at this age.

ORGANISM

The organism most frequently found in the joints of infancy is streptococcus hemolyticus with pneumococcus and staphylococcus aureus following in that order. Among other organisms found may be mentioned the meningococcus, the influenzal bacillus and the gonococcus; joint involvements due to the first two are usually secondary to a meningitis from the particular organism. Septic joints in which the organism is known to be the meningococcus need not be drained, but the patient should be treated with anti-meningococcal serum. Some advocate the use of serum in the joint. Likewise, gonococcal joints in children may be treated conservatively; they do much better than gonococcal joints in adults and have an excellent prognosis as to function.

The following case illustrates another answer to the problem of the sick child with a swollen painful extremity.

CASE II. J. M., aged one year, was admitted with a complaint of an acute illness of six days' duration associated with pain in the left lower extremity of five days' duration. General health previous to present illness had always been good, except for intermittent head colds for two or three months preceding the onset. The present illness came on with a high fever, and the day following the mother noticed that the child did not want to move his left leg, which was swollen in the region of the knee. At this time, four days before admission, the child was seen by the family physician, who had a roentgenogram taken which was found to show nothing abnormal. The diagnosis was not made at this time.

Examination at the time of admission showed a fairly well nourished, pale, dehydrated, acutely ill child. Except for these general findings and the presence of acutely inflamed tonsils the only significant findings were in the left lower extremity. The whole of the thigh and the proximal two-thirds of the leg were greatly swollen and the knee was held in a position of seventy degrees flexion. However, if the part was handled gently, motion at the knee joint was not particularly painful, except in the extremes of the arc of motion. The maximal tenderness and thickening were over the lower end of the femur. There was no evidence of fluid in the knee joint. The WBC was 26,000. The temperature was 103.4 degrees. The roentgenogram was negative except for the presence of swelling of the soft tissues. *Impression:* osteomyelitis of the lower end of the femur.

The extremity was immobilized and a poultice applied. The following day, through a lateral incision, pus was exposed in relationship to the lower end of the femur. The bone was not opened at the operative procedure. The wound was packed with vaseline gauze, and a plaster cast was applied which was bivalved to allow for subsequent dressings. The organism was staphylococcus aureus. Postoperative roentgenogram showed a destructive process in the lower end of the femur.

The child's temperature dropped to normal. Dressings were done infrequently and two months later the wound had healed.

DISCUSSION OF CASE; DISCUSSION OF DIFFERENTIAL DIAGNOSIS IN OSTEOMYELITIS

This is entirely typical of osteomyelitis in infancy. The severity of the illness may be extremely variable, from an overwhelming infection which may cause death in forty-eight hours to a benign low-grade process. Usually the local manifestations of the process develop more rapidly than in older individuals so that unless the child is seen early in the course there may be diffuse swelling of the entire extremity. We have seen the whole lower extremity swollen from an osteomyelitis of the fibula before the periosteum had ruptured.

Osteomyelitis starts in the metaphysis, which is adjacent to the joint, but ordinarily, as previously noted, it can be differentiated from a septic joint. In the particular case above, although the knee was held in flexion-deformity, with care relatively painless motion was carried out and no fluid was found in the joint.

Furthermore the maximal thickening and tenderness were over the lower end of the femur. However, one frequently cannot differentiate osteomyelitis and a "deep cellulitis" (or subfascial abscess). If the maximal swelling and tenderness are removed from the metaphysis it is suggestive of an infection in the soft tissues. The roentgenogram is usually of little aid in differentiation before the seventh to tenth day of the disease. Furthermore, even if osteomyelitis is recognized the extensive swelling makes it very difficult to define the location of the osteomyelitic lesion accurately. Inability to make accurate determinations as to tenderness increases the difficulty still further. It would be very unfortunate if it were true that an early diagnosis and immediate operation were essential in the treatment of osteomyelitis of infants. We do not believe that it is.

PROGNOSIS AND TREATMENT OF OSTEOMYELITIS; DIFFERENCES OF DISEASE IN INFANCY FROM THAT IN OLDER CHILDREN

In another paper we have pointed out that, if an infant does not die with the acute illness, the anatomical and functional prognosis of the disease is excellent. In the majority of cases the wound is healed in two months; it is rare for it not to be healed in four months. Recurrences are infrequent. Seldom indeed does the osteomyelitis of infancy adopt the chronic characteristics of osteomyelitis of older individuals.

Furthermore, in infancy osteomyelitis seems to do about as well when the process is allowed to localize and merely drainage of the "soft tissue abscess" is carried out, as when immediate operative procedure on the bone is done. Sequestration is rare in any instance.

We have explained the difference between osteomyelitis of infancy and that of older individuals by the difference in the anatomical construction and physiological characteristics of the bones in infancy, as well as by the fact that streptococcal osteomyelitis is twice as frequent as staphylococcal osteomyelitis at this age.

In view of these facts one should be sure of the site of a lesion before any surgery is done. An immediate operation is not the most important consideration. Even if the exact site of the lesion is recognized, one should not operate if it is contraindicated by the general condition of the patient as, for example, by the presence of an acute respiratory infection. With planned delay the part should be immobilized, a poultice may be applied, and general supportive therapy given. Normally the patient improves under this régime; at the same time one may more accurately recognize the lesion as the process becomes localized and an accurate surgical procedure may be carried out. The bone may be drained by means of a small window in it, but in many instances we drain only the "soft tissue abscess". Surely if the abscess is drained, one need not, if it complicates the procedure, search for the lesion in the bone.

It is our habit to pack open the wound with vaseline gauze and immobilize the part, repeating the dressings at not oftener than weekly intervals.

The following case, with a history rather similar to the two previously given, illustrates the difficulty of immediate diagnosis and the value of delaying the surgical procedure.

CASE III. C. B., aged nineteen months, was brought to the hospital with a complaint of an acute illness of three days' duration and a swollen left arm in the region of the elbow of two days' duration. The child had been well up to the age of nine months when it was noted that she chewed the paint from her crib and her toys; she had been irritable since that time. Two weeks before the present admission she had had an acute respiratory infection with a temperature as high as 103 degrees, but this had largely subsided before the onset of the present illness. The day of the onset she developed a high fever and had a convulsion. The day following it was noted that there was a swelling at the left elbow which was quite tender.

Examination at the time of admission showed a rather poorly developed, severely ill child with an acute respiratory infection. Local examination of the left upper extremity showed a diffuse swelling extending half way up the arm and downward to the middle of the forearm, more marked on the medial side, associated with definite redness and increased heat. There was no fluctuation and, although motions of the elbow were resisted, almost complete motion could be obtained without severe pain if the part was handled carefully. The temperature was 105 degrees. The white blood count was 29,350. Blood culture showed pneumococcus. Roentgenograms were negative except for the soft tissue edema and a definite lead line adjacent to the epiphysis. It could not be decided whether this was an osteomyelitis of the lower end of the humerus or a deep cellulitis.

The child's arm was immobilized and she was given general supportive therapy including therapy for plumbism. A bulging right ear drum was opened two days after admission. The child gradually improved. Nine days after admission the process had become localized and fluctuant and it was drained by a simple incision. The patient rapidly improved. The temperature dropped to normal and the wound was healed two weeks later.

When this child was first seen, the three possibilities—osteomyelitis of the lower end of the humerus, a "subfascial abscess", and a septic elbow were considered. She actually had a deep cellulitis—a subfascial abscess. Time made the diagnosis. The delay not only helped in the diagnosis but during the interim the child's general condition improved. Roentgenograms taken after the operation showed no evidence of osteomyelitis.

CONCLUSION: In conclusion I may say that the early differential diagnosis of the type of acute process in an extremity of an infant may be difficult. If the site of an infection cannot be accurately specified, or if operation is contraindicated by the general condition of the patient, planned delay of the surgical treat-

ment is the desirable course. The first step in this treatment is to *immobilize the part and treat the child.* Of the three more common types of acute infection in the extremity, soft tissue infection, osteomyelitis, and septic joint, the one that preferably should be drained relatively early is the septic joint. Fortunately it is the most easily recognized.

Early operation is not essential in the treatment of osteomyelitis of infancy and, of course, to allow localization of a soft tissue infection before it is drained is desirable.

Once the site of an osteomyelitic lesion is accurately recognized it may be drained by a small window in the bone, if the procedure is not otherwise contraindicated. However, they seem to do about as well when one awaits localization and drains the "soft tissue abscess" only.

Extensive poorly-timed surgery in lesions of the extremity in infancy (under two years of age) is to be decried.

DISCUSSION

CHAIRMAN COBB: The discussion of this paper will be opened by Dr. Frank R. Ober, of Boston.

DR. FRANK R. OBER: *Mr. Chairman and Members of the Society*—Dr. Green has made an excellent presentation of his subject and I wish to emphasize some of his points. We see a great many of these patients at the Children's Hospital, both in the infants' and the children's wards, with such infections. It is frequently the case that there is a history of antecedent infection, the most common being in the respiratory tract, the tonsils, the lungs, or the middle ear.

The importance of early diagnosis cannot be overemphasized, and it is easily missed as Dr. Green has pointed out. Quite often after these antecedent infections, the temperature stays up and it is quite difficult to determine what is going on in the individual patient. Examination of the extremities should always be made. When the first early sign appears we should not be content that it is the only place in the extremities affected. There may be multiple infections. Many have multiple septic joints, or multiple osteomyelitis. It is a curious fact that when joints are affected the multiple infections are usually those of the joints and in those of osteomyelitis they are usually those of the bone.

Many of these children arrive in the hospital very ill and dehydrated. Many years ago, I am sure, we lost many of these patients in our eagerness to operate. When the diagnosis of osteomyelitis was made, it was the custom to operate at once, removing a large piece of bone. The dehydrated child will not stand anesthesia very well, and he stands operations less well. It is not necessary to do operations on these cases early, but it is better to wait until the general condition has improved. It is sometimes difficult to decide whether it is a septic joint or an osteomyelitis. Osteomyelitis always occurs in the end of the bone, and the irritation from the infection may give synovitis of the neighboring joint. It is bad surgery to open up a joint and find nothing but a little fluid and then have osteomyelitis in the same area, later on getting a secondary joint infection as a result of that surgery. Since we have abandoned the policy of doing early operations and have waited until localization and a better general condition have resulted, the death rate at the Children's Hospital in these cases has been reduced from about fifty per cent to about five per cent in the last twenty-five years.

When one is going to operate on a small infant with serious infection, the operative preparations, including the operating room and the scrubbing up of doctors and nurses, should be made before the anesthetic is given. In this way we submit the child to the least amount of anesthesia possible and the result will be less shock. As little surgery as possible should be done and when pus is found in osteomyelitis, we should not attempt to remove a lot of bone but simply drain the pus cavity because we do not get the usual sequestrum in these infants under two years of age.

CHAIRMAN COBB: The second discusser of this paper is Dr. Henry W. Hudson, Jr., Boston.

DR. HUDSON: We are indebted to Dr. Green for a clear presentation of the problem of the acutely ill infant with a painful extremity. I find myself in harmony with much that he has expressed and wish to emphasize only one of his theses—that the care of the patient is of primary importance and must not be lost sight of in the local treatment of the extremity.

Some of us have been incorrectly quoted as opposing drainage in osteomyelitis. This is far from the truth, but is perhaps explained by the policy of systemic treatment first with local treatment as an important adjunct.

In this age group many infants are waging their first battle against pyogenic infection. Their defensive mechanisms have not been conditioned by the repeated infections, respiratory and otherwise, which are the common lot of older individuals. Time is necessary for the production of antibodies against the invading bacterial antigens. Not infrequently the infant is prostrated, has high fever, and his metabolism is altered by dehydration and ketosis. Efforts made to correct these aberrations require the expenditure of time, and the time is well spent.

The fact that osteomyelitis in infancy very regularly begins in the metaphysis adjacent to the epiphysis is both an aid and a handicap in diagnosing the lesion as one in bone, one in a joint, or one limited to the soft parts. Very frequently, early in the disease, there is marked edema and reddening over a wide area and it may be difficult or impossible to distinguish between cellulitis, osteomyelitis, or purulent arthritis. Operation at this time, without definite localizing signs, may result in unnecessary trauma, notoriously poor treatment of infection, and the contamination of tissues which otherwise might escape infection. Since the recovery of the patient and the healing of his infection are at stake, the soundest judgment in choosing time and manner of operation is essential.

Fortunately, as Dr. Green has pointed out elsewhere, the prognosis for the bone is good, providing the patient recovers. We will be wise, therefore, to treat the patient first and secondarily to provide drainage in the simplest, least destructive manner possible when localizing signs are evident.

CHAIRMAN COBB: Dr. Green, will you close, please?

DR. GREEN: I should like to make one statement only; by allowing an osteomyelitic process in infancy to localize, a minimal amount of surgery may be done with very good results.

CHAIRMAN COBB: This closes the program. All those in favor of extending a vote of thanks to all who took part in our program to-day, will please rise. (All rise.)

(Adjourned at 5:15 P.M.)

GASTRO-INTESTINAL ALLERGY AS A CAUSE OF INTESTINAL OBSTRUCTION

BY DAVIS T. GALLISON, M.D.*

THAT allergy may cause gastro-intestinal symptoms and recognizable lesions in the intestinal tract has long been realized. In 1645, and in 1649, Spigelius and Riolan noted in the cadaver narrowings of the gut which they termed "angry contractures" due to enterospasm[1]. In 1884, Johnathan Hutchinson recognized that certain foods would cause gastro-intestinal symptoms with some individuals but not with others[2]. In more recent years, Rackemann[3], Vaughan[4], Rowe[5], and numerous other investigators have stated that sensitivity to proteins of foods may cause various gastro-intestinal symptoms varying from mild abdominal discomfort to acute pain, nausea, and vomiting.

However, that these allergic symptoms may be severe enough to simulate intestinal obstruction (and indeed the reaction of the intestine may result in true obstruction) is not generally recognized by the profession. A search of the literature disclosed the report of only one case of obstruction due to allergy. Bogart[6] reports a case which came to operation in which the lumen of the jejunum was practically occluded by edema and swelling of the wall due to hypersensitivity. There is irrefutable evidence that such a reaction is due to allergy. Rackemann[7] states that vascular reactions due to allergy are capillary dilatation with increased permeability and exudation, and spasm of the arterioles. There may be various degrees of these reactions, varying from simple spasmodic contraction to actual edema.

In order to establish a diagnosis of allergy, certain criteria should be demonstrated:

(1) Previous history of allergic stigmata in the patient or in his immediate family, such as asthma, hay-fever, urticaria, angioneurotic edema, migraine, etc.

(2) Occurrence of the symptoms following ingestion of certain proteins.

(3) Relief of symptoms on omitting offending proteins from diet.

(4) Reproduction of symptoms on reingesting proteins.

(5) Demonstration of patients' sensitivity to offending proteins by skin tests.

(6) Increase of blood NPN and eosinophilia.

In the case to be reported, all these phenomena were demonstrated.

*Gallison, Davis T.—Instructor in Medicine, Tufts College Medical School. For record and address of author see "This Week's Issue," page 187.

CASE No. 0285. White male. Aged 29.

C. C. Acute abdominal pain, nausea, and vomiting.

P. I. Two hours after breakfast there was a sudden attack of severe epigastric pain, accompanied by nausea, vomiting, and a desire to defecate but with inability to do so.

P. H. Five similar attacks had occurred during the previous year, but none so severe as this one. Numerous attacks of hives during youth.

P. E.

T	P	R	BP
99	88	20	138/90.

Patient was suffering acute abdominal pain, vomiting bile-stained fluid at frequent intervals. Abdomen was distended, tympanitic, and rigid with generalized tenderness. No visible peristalsis, but on stethoscopic examination there was marked hyperperistalsis above and to the left of the umbilicus.

Treatment:

The patient was given morphia gr. 1/4 sc. and a milk and molasses enema. The morphia had little or no effect. The enema produced a poor fecal result and no gas. It was noted that there was a large urticarial wheal where the morphia had been injected. Further investigation disclosed the presence of marked dermographia. These findings suggested an allergic condition as a basis for the symptoms. The administration of eight minims of adrenalin[8] was soon followed by relief of the pain, and another enema produced good gas results with disappearance of the distention.

Blood was taken for chemistry and morphology.
NPN—52 mg. per 100 cc.
Smear—8 per cent eosinophilia.

The patient was put on liquid petrolatum therapy[9] and advised to report for skin tests.

Three days later the patient had another similar attack which was relieved by the same methods. He had not taken any petrolatum in the meantime.

At a later date, the patient was skin-tested to the various food proteins, and prunes and eggs (ovomucoid) were found to be the offenders. These were omitted from his diet and he was symptom-free for a month. He then volunteered to ingest the offending proteins. A meal consisting of six stewed prunes, a soft boiled egg and toast was followed two hours later by a severe gastro-intestinal upset, characterized by pain, nausea, vomiting and distention. The symptoms were again promptly relieved by adrenalin and an enema.

SUMMARY

(1) A brief résumé of the history and symptoms of gastro-intestinal allergy is given.

(2) A case of partial intestinal obstruction due to allergy is described.

COMMENT

The writer feels that the possibility of gastro-intestinal allergy should be considered, especially in those cases of intestinal obstruction in which the symptoms of organic lesions are not clear-cut.

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CANCER OF THE PANCREAS

BY FREDERICK L. HOFFMAN, LL.D.*

WHILE there are innumerable observations on cancer of the pancreas, this particular type of malignant disease does not appear to have heretofore received extended statistical consideration. Most of the references to its occurrence are based on fragmentary data insufficient for the purpose of a final conclusion. Ewing remarks in his treatise on Neoplastic Diseases that,

> "Cancer of the pancreas formed 1.76 per cent. of Kaufmann's autopsies on malignant tumors. Of 2943 autopsies on cancer referred to by Korte, there were 59 pancreatic cases (2 per cent). Bashford collected 1000 cases of primary malignant tumors of the pancreas among 84,000 cancers. Owing to the difficulty of accurate diagnosis the value of miscellaneous statistics may be doubted. Ollivier has pointed out the necessity of very careful histological study, in order to avoid confusion with cancer of the duodenum and bile-ducts."

The foregoing statement fails to take account of the apparent increase in cancer of the pancreas during recent years. Walshe in his classical treatise on The Anatomy, Physiology, Pathology, and Treatment of Cancer, Boston, 1844, gives a table of cancer deaths in Paris by organs and parts, according to which out of 9,118 deaths from all forms of cancer, twelve were from cancer of the pancreas, ten being male deaths and two female deaths. Walshe in his larger work on The Nature and Treatment of Cancer, London, 1846, enlarges upon cancer of the pancreas to a considerable extent, including many important observations introduced by the statement that, "The pancreas is among the rare sites of cancerous formation."

Stout in his observations on cancer of the pancreas remarks that,

> "Since it is an internal cancer it is very difficult to estimate its actual incidence, both because many cases probably die undiagnosed and because when it becomes large and involves surrounding organs it is often impossible to recognize the tissue of origin. During a ten-year period at the Presbyterian Hospital 33 primary cases were recognized among 1862 cancers of all kinds, percentage of 1.77. Neither sex shows a preponderance and, as in most carcinomas, it is distinctly a disease of the later years of life; 76 per cent of the cases studied by us had passed the fifth decade of life."

More conclusive are the statistics of the United States Census Office which cover the period 1915-1932. In 1915 the death rate for cancer of the pancreas in the United States registration area was 1.1 per 100,000, increasing progressively to 1.5 in 1922 and 2.8 in 1932. How far this increase is actual or the result of improved diagnosis cannot, of course, be stated but the latter factor unquestionably plays some part in the larger observed incidence of the disease at the present time. It is probably safe to assume that when all allowance is made for perfection of diagnosis, the present mortality from cancer of the pancreas is not less than three per cent of the total mortality for all forms of malignant disease in the United States.

The actual mortality from cancer of the pancreas in 1932 in the United States registration area, which includes practically the whole United States with the exception of Texas, was 3,361. Again making allowance for errors in diagnosis and missing returns for a few states, the probability is that cancer of the pancreas causes not less than 4,000 deaths in the United States at the present time. Hence one can no longer speak of cancer of the pancreas as a rare disease, as will be shown by a few comparative statistics. While cancer of the pancreas in the United States registration area in 1932 caused 3,361 deaths, cancer of the esophagus caused 2,058 deaths, lungs and pleura 3,156, ovary and Fallopian tube 2,160, all types of cancer of the skin 3,120, and finally cancer of the prostate 5,438. I give below for convenient reference a table showing the death rate from cancer of the pancreas by single years 1915-1932.

CANCER OF THE PANCREAS,
U. S. REGISTRATION AREA,
1915-32

	Rate per 100,000				
1915	1.1	1921	1.5	1927	2.2
1916	1.2	1922	1.5	1928	2.3
1917	1.2	1923	1.7	1929	2.4
1918	1.2	1924	1.8	1930	2.5
1919	1.2	1925	1.8	1931	2.6
1920	1.3	1926	2.0	1932	2.8

*Hoffman, Frederick L.—Member of Board of Directors of the American Society for the Control of Cancer. For record and address of author see "This Week's Issue," page 187.

Since 1915 the total number of deaths from cancer of the pancreas in the United States registration area has been 33,125. It is self-evident that this considerable mortality is deserving of much more attention than has heretofore been given to it, both as to causation and treatment. I may say in this connection that in 1920 the proportion of deaths from cancer of the pancreas in the total mortality for all forms of cancer was 1.6 per cent, increasing to nearly 3 per cent by 1932.

Comparing the American death rate for cancer of the pancreas with that of England and Wales for recent years, I am able to give the following returns: For both sexes combined the death rate for cancer of the pancreas increased from 2.21 in 1921 to 3.87 in 1930. For the two sexes separately, however, the data are more interesting. For males the death rate from cancer of the pancreas increased from 1.45 per 100,000 during 1901-10 to 1.67 during 1911-20, to 3.40 in 1926 and to 4.11 in 1929, decreasing to 4.04 in 1930. For females the rate increased from 1.18 per 100,000 in 1901-10 to 1.31 in 1911-20, 3.05 in 1926 and 3.72 in 1930. It appears therefore that in England and Wales the death rate for cancer of the pancreas is slightly less for females than for males.

I am able, however, to amplify the foregoing by some exceptionally interesting statistics, collected in connection with my San Francisco cancer survey, which represent an analysis of 66,402 deaths from cancer in some twenty different localities and areas of the United States and Canada. The total number of deaths from cancer of the pancreas in this group was 1,264 as compared with 1,533 for the lungs, 1,677 for the bladder, 1,683 for the prostate and 1,887 for the esophagus. The number of male deaths from cancer of the pancreas in this group was 738 and that of females, 526, so there is a lesser incidence of cancer of the pancreas among women than among men in this country at the present time. The average age at death in cancer of the pancreas was 59.6 years for both sexes combined or respectively 59.3 years for males and 60 years for females. The average known duration of the disease for both sexes combined was 10.4 months or respectively 9.5 months for males and 11.5 months for females.

My San Francisco cancer survey also reveals some extremely interesting comparative rates of mortality from cancer of the pancreas in different sections of this country and Canada, as shown in the table following:

MORTALITY FROM CANCER OF THE PANCREAS

RATE PER 100,000

	Persons	M.	F.
San Francisco, 1924-27	4.4	5.0	3.8
San Francisco, 1928-31	4.7	6.5	2.7
Oakland, 1924-28	3.2	2.7	3.7
Chicago, 1925	3.1	3.5	2.8
Buffalo, N. Y., 1922-26	2.4	2.8	2.1
New Orleans, white, 1919-23	0.8	1.2	0.5
New Orleans, colored, 1919-23	0.4	0.4	0.4
Virginia, 1926, white	1.6	2.1	1.1
Virginia, 1926, colored	0.8	1.1	0.6
East Orange, N. J., 1931-33	2.3	2.0	2.6
Albany, N. Y., 1924-29	4.5	5.9	3.2
Hawaii, 1924-28	1.4	2.0	0.6
Hawaii, 1928-31	0.9	0.7	1.3
British Columbia, 1920-24	2.1	2.7	1.5
British Columbia, 1925-29	2.9	3.3	2.5
Alberta, 1921-25	0.8	0.8	0.9
Saskatchewan, 1920-24	0.7	0.6	0.7
Winnipeg	2.3	2.5	2.2
Hot Springs, 1914-26	2.6	2.7	2.6
Hot Springs, 1927-31	1.0	2.1	—
Madison Co., N. Y., 1919-32	0.8	1.0	0.8
Amsterdam, Holland, 1920-29	0.8	0.9	0.7
Portsmouth, England, 1909-25	1.4	2.3	0.5
Montreal, 1909-25	0.9	0.9	0.8
Manila, 1924-28	0.6	0.7	0.4

It is thus shown that there are wide variations in the local incidence of cancer of the pancreas, the causes of which at the present time are unknown. The available facts, however, suggest a further study which should be based on original death certificates, with all the facts given on the certificates taken into account.

Cancer of the pancreas is rarely reported separately for most of the countries for which vital statistics are available. For the Irish Free State statistics have been published for a period of years according to which, for 1924-31, the male death rate for cancer of the pancreas was 1.8 per 100,000 while the female rate was 1.2. For other localities the rates have been as follows:

MORTALITY FROM CANCER OF THE PANCREAS

RATE PER 100,000

	M.	F.
Northern Ireland, 1926-32	2.0	1.6
Switzerland, 1926-30	2.4	1.9
" " Zurich	2.4	2.0
" " Berne	2.7	1.2
" " Tessin	3.9	4.3
" " Vaud	2.5	1.5
" " Geneva	3.2	2.4
Australia, 1903-23	1.6	1.1

It would be interesting to extend this international comparison, but as I said before, the data are difficult to secure. I have a return for Rangoon, Burma, for the period 1926-32, according to which there were 296 deaths from cancer of all forms, of which only one was from cancer of the pancreas. This conforms to an analysis I made of the cancer specimens examined at the Medical Research Institute of the Federated Malay States for the years 1926-31. This analysis included 654 deaths from cancer, all forms, of which only two or 0.3 per cent were deaths from cancer of the pancreas. These were male deaths.

I also have a special return for Manila, 1924-28, based on an examination of original cancer death certificates, representing 760 deaths or respectively 383 males and 377 females, of which six or 1.6 per cent were deaths from cancer of the pancreas in males and three, or 0.8 per cent, were deaths of females. Finally, I have

an interesting return based on original data furnished by the government of Palestine representing 352 deaths from all forms of cancer during 1931-32, of which seven were from cancer of the pancreas, or respectively out of 177 deaths of males, four were cancer of the pancreas, and out of 175 deaths of females, three were from this type of the disease.

Through the kindness of the Director of Vital Statistics I have obtained a statement of deaths from cancer of the pancreas for the registration states of 1920 for the year 1931 which I give in the same form as shown for England and Wales.

DEATHS FROM CANCER OF THE PANCREAS, U. S. REG. STATES OF 1920, 1931

Age	Deaths	Age	Deaths
Under 35	61	60-64	464
35-39	64	65-69	446
40-44	128	70-74	401
45-49	199	75-79	238
50-54	313	80-84	104
55-59	404	85 and over	43

This statement may be amplified by some additional observations on cancer in early life. There were two deaths from cancer of the pancreas under five years of age, one at three and one at four. There was one death at ages five to nine, one at ten to fourteen, three at fifteen to nineteen, eight at twenty to twenty-four, eleven at twenty-five to twenty-nine, and thirty-five at thirty to thirty-four, a total of sixty-one deaths at ages under thirty-five. Out of a total mortality of 2,867 from cancer of the pancreas in the registration states of 1920 in 1931, 1,508 were white males and 1,263 white females, while there were fifty-three colored males and forty-three colored females. There is therefore sufficient reason for believing that cancer of the pancreas is much less common among the colored than among the white population. This statement is supported by my special returns for New Orleans and Virginia given in full detail in different sections of the San Francisco cancer survey.

I know of no extended statistics of cancer of the pancreas according to the precise seat of the disease in the organ affected. According to Ewing, "The location of the tumor is usually in the head or extending diffusely over most of the organ. Tumors limited to the body are much less common, and the tail is rarely affected. Of 386 cases collected from the literature, 158 were diffuse, 156 limited to the head, twenty-eight in body, and twelve in tail. The organ is regularly enlarged, but in scirrhous tumors it may be small but very hard."

David Krestin, in a review of his paper on Diseases of the Pancreas in the *American Journal of Cancer* for May, 1932, is quoted to the effect that, "Eighty per cent of pancreatic cancers occur in the head of the organ. The incidence is greater in males. The symptoms and signs of pancreatic cancer are increasing obstructive jaundice, rapidly progressing emaciation, cachexia, anorexia with a distaste for fats, pain in the left hypochondrium or back when the celiac plexus is involved, diarrhea with characteristic pancreatic stools, painless enlargement of the gallbladder, and evidence of pancreatic inadequacy."

For most of these observations definite data are apparently not available but there is no disagreement on the part of authorities that jaundice is one of the most characteristic symptoms in the early onset of the disease.

With further reference to the relative frequency of cancer of the pancreas, I quote the following observations from Osler's Principles and Practice of Medicine, Eleventh Edition, 1930,

> "At the General Hospital, in Vienna, in 18,069 autopsies there were 22 cases of cancer of the pancreas (Biach). In 11,472 post mortems at Milan, Segre found 132 tumors of the pancreas, 127 of which were carcinomata, 2 sarcomata, 2 cysts, and 1 syphiloma. In 6,000 autopsies at Guy's Hospital there were only 20 cases of primary malignant disease of the organ (Hale White). Among 42,000 admissions to the Johns Hopkins Hospital, Futcher reports 58 cases in which a clinical diagnosis was made; in 31 of these the diagnosis was verified by operation or autopsy. The head of the gland is most commonly involved, but the disease may be limited to the body or to the tail."

In the same discussion occurs the statement that, "Of new growths in the organ, carcinoma is the most frequent. Sarcoma, adenoma, and lymphoma are rare. Adenoma of the islands of Langerhans may cause hypoglycaemia (hyperinsulinism)." Cases of carcinoma of the pancreas originating in the islets of Langerhans are occasionally reported in the literature, but they apparently are relatively rare. The work of Seale Harris on hyperinsulinism may be referred to as suggestive of a new line of approach for diagnostic purposes. George T. Pack, in reviewing carcinoma of the islets of Langerhans, by Cottalorda and Escarras in the *American Journal of Cancer*, December, 1933, gives the following details of more than passing interest:

> "A thirty-two-year-old woman had been aware for two months of a slowly growing tumor in the left hypochondrium. Radioscopic studies of the digestive and urinary systems were normal. An exploratory laparotomy revealed a tumor the size of two fists, attached to the posterior abdominal wall and originating from the tail of the pancreas. The tumor was successfully extirpated and had not recurred nine months later. Cornil made the microscopic examination and found the tumor to be comprised of endocrine cells, typical of the islets of Langerhans. The patient never had hypoglycemia."

To these observations Pack adds the following note: "Seale Harris, who first discovered and named the endocrine imbalance known as hyperinsulinism, has recently observed a significant relationship between these tumors of the islets of Langerhans (insulomas) and certain types of epilepsy (*J. A. M. A.* 100: 321, 1933). The epileptiform seizures occur during the hypoglycemic state and may be prevented in some patients by an appropriate diet."

Mention may also be made of the discussion on Carcinoma of the Pancreas by K. Masumoto reviewed by Cavers in the *Cancer Review*, 1932, to the effect that "In a series of 2,420 necropsies the author observed 14 cases of carcinoma of the pancreas out of a total of 275 carcinoma cases. The most frequent and prominent symptom was ascites, found in 12 cases and attributed to portal stasis and peritoneal carcinomatosis. Histologically it could not be ascertained whether the disease arose in the islands of Langerhans or in the duct epithelium."

With reference to the rarity of primary sarcoma of the pancreas, I quote a brief review of the discussion by Tscherepnina, made by Cavers in the *Cancer Review*, 1931.

> "The author emphasizes the rarity of primary sarcoma of the pancreas; he found 50 cases reported in the available literature. His patient was a man of 51 who entered hospital in January, 1930; no operation was done, and death occurred 2 months later. At necropsy, a tumour was found in the head of the pancreas; it had grown through Wirsung's duct into the duodenum and compressed the portal vein, and was a polymorphic-celled sarcoma with numerous mitotic figures. The whole pancreas was sclerotic, while the liver showed cirrhosis and atrophy. The author suggests that the sarcoma had arisen from antecedent inflammation of the pancreas."

Regarding adenomas of the islets of the pancreas, the work of C. Natali of the University of Pathological Anatomy, Florence, is reviewed in the *Cancer Review*, 1930, as follows:

> "The author describes a case of so-called adenoma of the pancreas. This occurred in a person of 60 years with adenocarcinoma of the stomach, and formed a nodule as large as a nut, of sulphur-yellow colour, projecting from the surface of the tail of the pancreas. Microscopically it was formed of cells of the islets of Langerhans, and showed a well-defined fibrous capsule. After giving a description of the microscopic appearances of the nodule the author gives a table of 19 cases of a similar nature compiled from the literature. In 16 out of the 19 cases diabetes was absent. He describes the variations and morphology of these structures and notes that hyaline degeneration in the walls of the vessels and in the stroma is common. He discusses the genesis of these islands of Langerhans cells, and inclines to the view that they are hamartomas. He believes that they are probably not functional and considers that they should be divided into two groups—those formed of islet tissue only, and those containing excretory ducts, the latter being at a lower stage of development than the former."

The reference to diabetes is suggestive and I hope some time in the future to be able to review the evidence regarding the probable correlation of diabetes to cancer, particularly of the pancreas, but this on the present occasion would carry me too far. The evidence apparently is quite conflicting. For the purpose of reasonable completeness in the present discussion I add a review of a discussion on diabetes in relation to cancer of the pancreas by Rothmann, reviewed by Rivero in the Abstract Section of the *American Journal of Cancer*, January, 1932, as follows:

> "The author presents a case of carcinoma of the pancreas with symptoms and signs of complete obstruction of the common bile duct and associated diabetes. Statistics are given to show that an association with diabetes exists in about 20 per cent of cases. In some cases the diabetes disappears as the state of carcinomatosis progresses. In this connection Rothmann states that it has been shown that the acini and islands of Langerhans are supplied by the same capillaries, that in certain pathologic conditions the capillaries become permeable to trypsin, and trypsin inactivates and then destroys insulin. Injections of trypsin in the pancreatic duodenal artery produce hyperglycemia and glycosuria by inactivation of insulin. Certain cases of diabetes may be explained, therefore, as follows; in a pancreas where there is pancreatic juice retention, the trypsin gets into the blood stream and inactivates the insulin, but as the acini are further destroyed and the trypsin disappears, so does the diabetes."

Diseases of the Pancreas.—The relative mortality from other diseases of the pancreas is considerably less than that from cancer of the pancreas. In 1932 in the United States registration area, the total number of deaths from diseases of the pancreas was only 677 against 674 in 1931 and 668 in 1930. The death rate from diseases of the pancreas was 0.6 per 100,000 in 1932 compared with a rate of 2.8 for cancer of the pancreas for the same year. In other words to every death from diseases of the pancreas there are 4.7 deaths from cancer of the same organ. The available space precludes an extended discussion of this disease which involves many highly complex aspects for both diagnosis and treatment. I give first a table for diseases of the pancreas in the United States registration area, 1921-1932.

DISEASES OF THE PANCREAS,
U. S. REGISTRATION AREA,
1921-1932

Rate per 100,000

	Deaths	Rate
1921-24	2,062	0.54
1925-29	3,345	0.61
1930-32	2,039	0.57

In England and Wales the death rate for diseases of the pancreas increased from 0.4 per 100,000 in 1911 to 1.3 in 1932, the highest rate on record. The actual mortality during this period was 5,797, of which 2,797 were males and 3,100 females. In 1932 the rate was the same for both sexes, or 1.3 per 100,000.

I have also calculated the mortality rate for diseases of the pancreas in Australia for the period 1922-1932. In the aggregate there were 770 deaths from diseases of the pancreas, of which 299 were males and 471 females. The excess in mortality for females throughout the period under review is suggestive of fundamentally different conditions common to England and Wales and the United States. There was, however, a marked increase in deaths from diseases of the pancreas among males during recent years and a slight decline in the mortality among women. The rate per 100,000 was 0.96 for males and 1.58 for females.

For Canada I have information for the last five years showing no pronounced tendency toward an increase and with practical equality among the sexes. The number of deaths from diseases of the pancreas during the period 1929-32 was 237, or respectively 121 for males and 116 for females. The population of Canada at the present time is about 10,000,000 which would yield an average rate of 0.47 per 100,000.

An excellent discussion on diseases of the pancreas, illustrating their complexity, is contributed by Dr. E. W. Archibald to the Reference Handbook of the Medical Sciences, 1917. Dr. Archibald differentiates pancreatitis, acute necrosis of the pancreas, chronic interacinar pancreatitis, pancreatic calculi, pancreatic cysts, and pancreatic tumors.

We have practically no accurate information concerning the numerical distribution of the different types of the diseases suggestive of their relative frequency at the present time. With regard to cysts of the pancreas, Archibald observes, "It is probable that cysts of the pancreas are rather more frequent than was formerly supposed. While the number of recorded cases is not very large, it is safe to say that every hospital of late years contains records of cases that have never been published."

I have carefully examined the reports for the last ten years of the Medical Superintendent of the Registrar General's Office, London, which contain the only data on the subject with which I am familiar. They give a record of ninety-nine deaths from pancreatic cysts during the period 1921-1930, of which thirty-two were males and fifty-seven females. Non-differentiated non-malignant tumors of the pancreas numbered sixty-four during the same period, of which thirty-two were males and thirty-two females. I regret that I have no corresponding information for this or any other country.

Next to pancreatitis is the question of trauma which no doubt occurs with sufficient frequency to indicate its etiological importance. A third very important factor is gallstones mentioned by a number of authorities as a direct causative factor.

As regards acute pancreatitis Cecil, in his Textbook of Medicine, remarks that, "The disease appears to be more common in adult males who eat and drink heavily." I am unable to say which of the two forms of the disease is the more common. The late Dr. John B. Deaver was of the opinion (1917) that "the importance of pancreatitis was only lately becoming appreciated, but that it was the cause of many of the most severe gastric symptoms". Korte and Barker in 1917 were of the opinion that "males outnumber females in the ratio of 2:1". In this particular series of cases 76 per cent of the patients were females. According to Linder (1917), "The most potent factor in the causation of acute pancreatitis is, no doubt, gallbladder disease, including cholelithiasis."

SUMMARY. It is shown that cancer of the pancreas in the United States Registration Area was the cause of 3,361 deaths in 1932, while diseases of the pancreas during the same year caused 677 deaths. It is also shown that the mortality from cancer of the pancreas is on the increase but the rates for the different countries vary within comparatively narrow limits, as a general rule, the rates being higher for males than for females.

The average age at death from cancer of the pancreas in this country was 59.6 years for both sexes combined or respectively 59.3 years for males and 60.0 for females. The average known duration of the disease was 10.4 months for both sexes or 9.5 months for males and 11.5 for females.

It would seem well worth while to initiate a more comprehensive study of the geographical distribution of cancer of the pancreas and diseases of the pancreas in different countries of the world in view of the apparently increasing death rate from cancer of the pancreas during recent years.

RESECTION OF THE LOWER END OF THE ULNA (SUBPERIOSTEAL)

BY FREDERIC JAY COTTON, M.D.,* AND GORDON MACKAY MORRISON, M.D.*

PRIMARILY designed for wrists in which complicated fracture of the lower end of the radius has left the ulna overlong, with impingement on the carpus, this operation has other uses.

Sometimes a real Colles's fracture (not the type referred to above) shows a similar impingement. Sometimes a recurrent slipping of the ulnar head after wrist fracture may best be dealt with in this way, and in the cases of protruding ulna with a radius short from checked epiphyseal growth, it works out ideally.

Probably because no one ever writes about it, it is but little used, and the course of repair, and end results are not familiar.

The technique is simple enough:—a cut about three inches long on the inner side of the ulna from the wrist joint upward brings us to an area where the bone is uncovered. A longitudinal cut from wrist up, say 2½ inches, makes it possible to shell off the periosteum.

The bone is then cut, not with a chisel, because of trauma and the chance of splintering, but with narrow-nosed rongeur forceps, at a height about an inch and a half from the styloid tip, in such fashion as to leave a somewhat conical proximal stump. The near end of the distal portion is then grasped with bone-holding forceps, and lifted out, while the bone is cleared out from the periosteal sleeve with a curved "raspatory". Save where the ulnar extensor tendon lies in a groove next the styloid process, the separation is easy.

The wrist joint is opened up at the ulnar side but needs no attention. The periosteum, now a collapsed sleeve, is caught together with a couple of catgut stitches. No named vessels are cut. Nothing more is needed than the skin stitches and a pressure dressing. The astonishing thing about the manoeuvre is the repair. We have done it many times—have yet to see any joint reaction, and have always been surprised at the oddly good cosmetic result.

The collapsed, but substantially intact, periosteal sleeve lays down enough bone with scar-continuation to the old internal lateral ligament, so that the wrist is stable and strong. The new head is smallish, but not conspicuously so.

The operation, of course, in no way replaces the osteotomy still so often needed for recurring or *oftener, unreduced* deformity in Colles's fracture. Within limitations of indication, as above noted, however, it is extremely satisfactory.

O. W. J., seen February 6, 1933. Roofer. Aged 32. On December 16, 1931 fell through a skylight, fractured head of the radius at the elbow and dislocated the ulna (same arm, right) at the wrist.

Head of radius removed the day after the accident. Usual physiotherapy and leather support. Finds hand without strength and not fit for work. Shows scar over site of radial head. Pronation free, supination only 40 per cent. Ulna at wrist prominent, not loose, much too long for the shortened radius and impinging on side and especially at back of the carpus. The extra length and projection downward at least 1 cm.

Operated at the Faulkner Hospital. Cotton-Morrison, March 4, 1933. Seven-eighths of an inch of ulna removed subperiosteally, usual technique of closure. Examined May 5, 1933. Shows "unbelievably, no deformity whatever that one would notice. Even the prominence of the head of the ulna, or a corresponding prominence, not where it was but at the normal level, is visible." Motion at that time "pretty nearly normal" in all directions. He lost headway after this from an intercurrent illness. By October fifth, all wrist motions were free. There was still some limitation of rotation seemingly at the elbow.

*Cotton and Morrison—For records and addresses of authors see page 817, issue of April 12, 1934.

SOME PRESENT-DAY CONCEPTIONS OF PHOTOTHERAPY*

BY FRANKLIN P. LOWRY, M.D.†

THIS paper is compiled in part from the author's modest clinical opportunities, but is chiefly the results of work by men of high standing in their various professions.

Its sole purpose is to present these facts in an impartial manner and thus to acquaint the physician with the real value of the several types of therapeutic lamps.

DEFINITION

Phototherapy is the treatment of pathological conditions by means of ultraviolet, visible and infra-red radiations or vibrations given off from their source in the form of ether waves.

It must distinctly be borne in mind that "ultraviolet" and "infra-red" refer to certain definite spectral rays and are not confined in any sense to any particular make of lamp or element. Some rays from both of these groups are emitted from the sun and a reasonably large number of lamps in varying amounts.

HISTORY

From the dawn of history, man has realized the beneficial effects of light radiations. Many of the ancients laid great stress on sun treatment for their ills and even erected solariums. Hippocrates, the father of medicine, was sponsor of a health temple dedicated to "the sun, music and medicine".

The universal practice of sun baths, especially in the warmer climates, has continued until the present. However, nothing scientific was accomplished until the seventeenth century when Sir Isaac Newton, in 1666, discovered the spectrum of sunlight to be composed of violet, indigo, blue, green, yellow, orange and red rays. In 1678 Huygen announced the wave theory of light. Herschel discovered the infra-red spectrum in 1800 and the following year Ritter discovered the ultraviolet spectrum. One year later, Sir Humphrey Davy discovered the electric carbon arc. This was the beginning of artificial light therapy.

In 1889 Widmark, of Stockholm, proved that ultraviolet rays caused erythema and pigmentation of the skin. T. A. Palm, in 1890, wrote of curing rickets by sunlight. The first indubitable evidence of this was offered by Raczynski in 1912. During the years from 1892 to 1908 much was contributed by Arons, Hewitt, Kromayer and Nagelschmidt, to perfect the output of the mercury vapor quartz burner in common use to-day. Until his death in 1904, Finsen continued to work perfecting his carbon arc lamp which is to-day in constant use in the Finsen Clinic at Copenhagen. In 1903, Rollier opened the first clinic for systematized heliotherapy of surgical tuberculosis at Leysin, Switzerland. He has several lamps emitting approximately the sun's spectrum for emergency use on special cases during inclement weather. In 1920, ultraviolet radiation was used with success to clear up tetany.

During the first years of the twentieth century, most of the work in therapeutic lamps was carried on by individual manufacturers who were primarily interested in assembling lamps which would be salable and practical for use. Obviously, most of the treatments were necessarily empirical. It is only within the past few years that any considerable number of scientific workers in the laboratory and hospital have been engaged in earnest research in this most important field of sun and artificial light. To-day, by the increasing friendly coöperation of these two groups, much is being done in an attempt to establish a rational basis for the treatment of appropriate diseases by the proper type of radiation.

PHYSICS

All radiations have four definite and measurable properties; *wave-length, energy, penetration,* and *absorption.* Wave-lengths are readily and accurately determined by a spectroscope and are commonly measured in Angstrom Units (1/10,000,000 of a millimeter or 1/394,000,000 of an inch). Penetration is measured by photographic films and thermocouples.

It is possible that at some future time research may demonstrate also that each form of radiation consists of a definite quantity of energy. This is now a theory and called the "Quantum Theory".

Wave-length and energy depend entirely upon the source of radiation. (See table 1.)

Penetration and absorption depend not only upon wave-length and energy or intensity of radiation, but also upon the composition of tissues to be penetrated.

(A) Wave-Lengths

The wave-lengths of the spectrum as used in the treatment of disease (also including radium and x-ray) are as follows:

*From the Department of Physical Therapy of the Newton Hospital.
Presented at the meeting of the New England Physical Therapy Society on October 18, 1933.

†Lowry, Franklin P.—Chief of Department of Physical Therapy at the Newton Hospital. For record and address of author see "This Week's Issue," page 187.

TABLE 1

SUMMARY OF WAVE-LENGTHS OF ELECTROMAGNETIC SPECTRUM

(A—Angstrom unit)

Cosmic	Shortest
Gamma	Region of 0.1 A.
Roentgen	0.1 - 5.0
Ultraviolet extreme	Below 1,850 A.
" far or short	1,850 - 2,900 A.
" near or long	2,900 - 3,900 A.
Visible violet	3,900 - 4,500 A.
" blue	4,500 - 4,900 A.
" green	4,900 - 5,500 A.
" yellow	5,500 - 5,900 A.
" orange	5,900 - 6,300 A.
" red	6,300 - 7,600 A.
Infra-red near or short	7,600 - 14,000 A.
" far or long	14,000 - 90,000 A.

(The above measurements vary somewhat with the individual retina.)

TABLE 2

WAVE-LENGTHS OF DEFINITE KNOWN VALUE

Sunlight—2,900 - practically ends at 20,000 A.
Light visible to human retina—3,900 - 7,600 A.
Maximal erythema—2,970 A.
Tanning of skin—2,600 - 3,000 A.
Bactericidal (surface organisms)—2,000 - 2,900 A.
Absorption by Ergosterol (treatment of rickets) best at 2,800 - 3,200 A.

(B) Energy

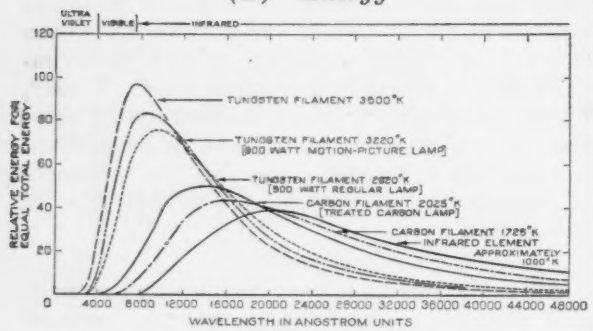

FIG. 1.

(Adapted from "Artificial Sunlight"—Luckiesh.)
K = Kelvin scale (Centigrade + 273).

Figure 1 illustrates the spectral distributions of *energy* from six sources, with their operating temperatures. It demonstrates graphically a well-established law of physics which states that the higher the temperature of the light source, the relatively greater the per cent of radiation emitted in the visible and near infra-red regions and therefore the deeper the penetration. In other words it shows that the hot tungsten filament lamp emits much more energy in the visible and near infra-red region than either the carbon filament lamp or the infra-red elements. It will therefore be seen that it is most important to use the proper source of energy for the results desired in penetration and absorption.

(C) Penetration

This is most important. Much of the value of phototherapy depends upon this property. Various kinds of tissue lie in the path of the rays and the distance reached by the latter is dependent on the nature of the tissue as well as on the wave-length and intensity of the rays. Ultraviolet radiations below 2,900 A. are absorbed in the atmosphere and therefore are only of theoretical interest. Small amounts of energy, from 2,900 to 3,900 A. are present in the sun's radiation. Ultraviolet rays with wave-lengths from 2,000 to 2,400 A. emitted from electric arcs are stopped in the stratum corneum or outer layer of the epidermis. (See fig. 2.) Those with wave-lengths from 2,500 to 3,300 A. pass through this layer, but are stopped in the stratum granulosum of the epidermis—that is, in the living epidermal cells. Those with wave-lengths from 3,400 pass through the entire epidermis but are stopped by the blood in the subepidermal capillaries. Rays with wave-lengths of 3,900 (these are the shortest visible light rays), probably do not penetrate farther than the longest ultraviolet rays. On the other hand, the visible red rays (wave lengths to 7,600) have a much greater penetrating power, some of them reaching the superficial strata of the muscles under the deep fascia before they are stopped. The visible green and yellow rays have an intermediate penetrating power. The near infra-red rays penetrate deeper than any rays of the spectrum but as they become longer they rapidly lose their power of penetration. The far infra-red rays have a very slight penetration, those beyond 14,000 being absorbed in the epidermis.

Unfortunately the rays which are most bactericidal (2,000 to 3,000) have a very feeble penetrating power. As the wave-lengths get longer the germ-destroying power falls rapidly. Consequently we cannot expect ultraviolet rays to destroy bacteria (that is, by direct action) except on the surface.

TABLE 3

TISSUE PENETRATION (APPROXIMATE)

1,900 - 2,500	Penetrates the epidermis (horny layer).
2,500 - 2,800	Penetrates the epidermis (pigment layer).
2,800 - 3,200	Penetrates the terminal blood vessel layer.
3,200 - 3,900	Penetrates the dermis proper.
3,900 - 10,000	Penetrates the dermis and subcutaneous layer.
10,000 - 14,000	Abrupt lessening of penetrating power to epidermis only.

The penetration of the various rays into human tissue varies somewhat according to the person and to the portion of the body irradiated. However, the following diagram will serve as an approximation.

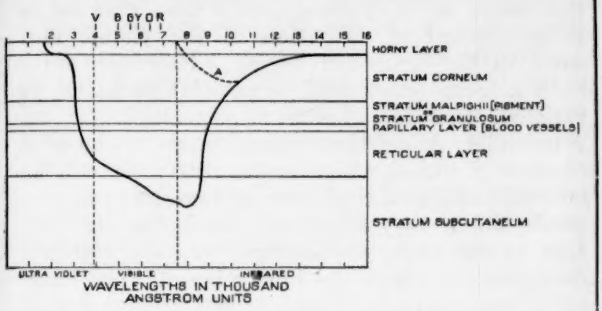

FIG. 2.

Much has been accomplished in the physics of the various types of radiations. It is now possible to accurately measure the wave-lengths of the radiations from the various burners and to have some idea of their penetration into human tissue. Many of the early clinical theories have been upset and lamps are being used more rationally as the results of these laboratory and clinical investigations.

Figure 2 very diagrammatically gives some idea of the penetration of the different portions of the spectrum into human tissues. This is of the utmost practical importance for it shows what is to be expected from any source of radiation of moderate intensity coming within this field (i.e., ultraviolet, carbon arc, tungsten filament or infra-red generators).

The radiations from an ultraviolet generator, theoretically, should be entirely below the 3,900 A. line but all these generators give off many bands in the visible and even a few bands in the infra-red.

The carbon arc output depends entirely upon the type of lamp and carbons. By using the proper carbons its output may extend over a portion of the ultraviolet, all the visible spectrum and continue through the infra-red well beyond 14,000 A.

Rays emitted from the infra-red "elements" follow approximately the line "A" (fig. 2) thus losing all of the great range of penetrating radiations found in some of the other lamps, but extending a long distance into the far infra-red region. The penetration of their rays into tissues is therefore extremely superficial.

(D) Absorption

When an impulse of light energy strikes the skin, one of two things happens; it either bounces off, in which case we say it is reflected; or else it sinks in, in which case we say the energy is absorbed. The absorption of light rays is the prime object of most of our body irradiation.

Absorption depends upon the result of the three previous properties of light—wave-length, energy and penetration.

Changes in body chemistry, increased blood supply in tissues, activation of hormones, etc., are all dependent upon the absorption of light energy. The depth of absorption depends of course on the penetration. Increased depth of penetration means increased depth of absorption, therefore deeper tissues are benefited when a more highly heated source of radiation is used.

This is demonstrated in table 4.

The human body is composed largely of water. With that fact in mind, the above investigations have been carried out by Luckiesh and others using water. Salts in solution, and other blood contents cannot alter conclusions based on the above facts. The effects of body tissues may alter the rays, but cannot change the above values relative to each other.

In table 4 are recorded percentage amounts of energy absorbed in four different thicknesses of water and the amount still remaining to penetrate and be absorbed at deeper levels. No data are available for comparison of an infra-red "element". However, these "elements" usually have a temperature of less than 1,000 K. with a penetration power proportionately less.

The foregoing reason, therefore, clearly demonstrates that from the standpoint of spectral energy, distribution, penetration and absorption, the tungsten filament lamp is apparently best fitted for therapeutic use where deep penetration without ultraviolet is desired.

The carbon filament lamp (such as that used in hand heaters) is next and the infra-red units of least value in fulfilling these requirements.

ACTION

The *ultraviolet rays* (the shortest of these therapeutic rays) are emitted from several types

TABLE 4

("Artificial Sunlight"—Luckiesh)

PERCENTAGE OF RADIANT ENERGY, FROM FOUR SOURCES, ABSORBED IN FOUR LAYERS OF WATER

Source (True Temperature)	Percentage of Total Energy Absorbed in Water of Depth				Remaining Unabsorbed at Depth of
	0.06 cm.	0.40 cm.	0.82 cm.	2.28 cm.	2.28 cm.
1) Carbon filament 2190 deg. K	64.1	77.3	81.0	87.9	12.1
2) Tungsten filament 2500 deg. K	50.4	64.5	70.5	80.0	20.0
3) Tungsten filament 2920 deg. K	46.5	58.0	62.2	70.5	29.5
4) Tungsten filament 3500 deg. K	33.6	43.6	48.4	56.4	43.6

1) Old treated carbon-filament; 4 watts per candle.
2) Approximating regular vacuum tungsten lamps; 9 lumens per watt.
3) Actually a 500-watt gas-filled tungsten lamp; 19 lumens per watt.
4) Near the melting-point of tungsten; 46 lumens per watt.

of lamps the most important of which are described below. They affect the chemistry of the body, by which certain body conditions are aided in recovery to normal. Just how improvement takes place we do not know except that it is apparently through some complex chemical or hormonic reactions. This has been made somewhat more specific by workers who have suggested that the clinical results from use of the ultraviolet rays are caused by the absorption of products formed by irradiation of body tissue cells and by non-specific protein reactions of an undetermined nature.

These rays have no heat or visibility. They are divided into the far (or short) and near (or long). The shorter rays are abiotic or tissue destroying. These also have the ability to kill surface bacteria. We are now beginning to realize what has long been a theory with conservative physical therapists, that the long continued exposure to short ultraviolet radiations can cause an aging of the skin if nothing worse.

The longer ultraviolet rays—those near the visible spectrum—are the ones which apparently are of more benefit to us in the treatment of diseased tissues. It is in this region that we find a narrow band which aids best in the cure of rickets. Rays from this region are also the indirect cause of erythema and tanning of the skin.

Next in order of wave-lengths are the *visible rays,* violet, blue, green, yellow, orange and red. As yet we are uncertain just what part visible rays play in our life history. We know that the violet end of this spectrum carries on some of the body chemical reactions ascribed to the ultraviolet rays. The longer rays—orange and red—are apparently chiefly concerned with heat and penetrate well into the tissues causing a stimulation of normal body functions. It is probably more than a conjecture that the other rays will some day be found to have a definite rôle in the chemical changes of the body necessary for our best good. This visible spectrum, while not directly necessary to the life of man, is indirectly of the utmost importance as upon its presence depends the development of chlorophyl, the basis of all life.

The one known value of the *infra-red rays* is that they heat body tissues. They have no known bands of emission of special curative value as is possibly the case with ultraviolet radiation. There are two types of rays, near or short (near the visible spectrum 7,600-14,000 A.) of decided penetration and far or long (14,000 and beyond) which hardly penetrate deeper than the horny layer of the skin.

SOURCES

(1.) The quartz vapor arc lamp is one of our most widely used generators for giving us our greatest range and penetration of ultraviolet radiation. It must be borne in mind that while the above is true, these lamps also give off a large amount of radiation in the visible and some in the infra-red region. However, since such a large amount of ultraviolet radiation is emitted, this lamp is used especially for its ultraviolet properties which seem to have a distinct chemical effect in the body. It will be noticed in figure 2 that these ultraviolet rays penetrate but a very short distance below the surface of the skin; the shortest (1,800-2,900 A.) do not reach below the horny layer. The longest or near ultraviolet rays (2,900-3,900 A.) penetrate the corium or derma, the dense connective tissue.

(2.) There are several lamps manufactured for general office use whose output is monochromatic, that is whose major output is in a single band with its wave-lengths in the region of 2,537 A. While lamps with this output are undoubtedly of some value, so far they have not been demonstrated to be of any more benefit than some other lamps. Moreover we do know that rays in this region are primarily destructive to human tissue. As yet very little is known about this band. With continued use its possibilities for harm seem greater than those for good. It certainly should not be used promiscuously on patients.

(3.) Carbon arc lamps are manufactured in many types. There are small ones using 10 or less amperes (the common office and "home treatment" types). These are cored carbon electrodes containing combinations of metal in order to produce several varieties of spectra. Really efficient results may be expected from those lamps using 20 or more amperes. These may use relatively plain composition carbon electrodes emitting a close approximation of the sun's spectrum and are very efficient. Cored carbon electrodes with various fillers are also used. Lamps using from 50 to 125 amperes are used in hospitals for the irradiation of several patients at the same time. With plenty of time and a solarium ventilated and arranged properly, these lamps produce notable results. Such work, however, is largely confined to Europe and most especially to Copenhagen. The Finsen Clinic in that city is world famous and its work to a very large degree is concerned with use of the carbon arc lamp treatments. These treatments usually average one and a half hours.

The chief objection to the use of the carbon arc lamps is that they produce much heat, glare, noise and odor. They require lengthy treatments and are thus expensive to operate. Because of these objections, even though the proper type of carbon is capable of emitting a most valuable spectrum for therapeutic use, the carbon arc lamp has never become a great favorite in this country.

(4.) The common incandescent lamp gives an output closely resembling the sun's spectrum

without the ultraviolet, but with visible and deep penetrating infra-red and some superficial infra-red rays. This makes an ideal lamp where penetration as well as superficial heat is desired. With this is also combined the entire visible spectrum.

(5.) Infra-red "elements" (non-luminous sources). Laboratory workers definitely state that the only attribute which has been found or is expected to be found for the infra-red unit giving off no visible spectrum, is heat. These elements emit very little of the near infra-red rays (7,600-14,000 A.) in the deeply penetrating region. Their chief output is in the region of the far infra-red (14,000-50,000 A.) which penetrate but little below the outer horny layer. Their possibility of heating any deeper is by the conduction of heat as in the case of a hot water bottle. As such a large amount of radiation is held in the surface layer of the skin, the skin becomes heated much more quickly than when other lamps of a more penetrating type are used. The chief objection to the use of these "units" or "elements" is their lack of deep penetration. However, if rapid superficial heating is desired, they are very satisfactory.

(6.) There are several types of "sun" or "health" lamps on the market, whose ultraviolet radiation is greatly emphasized. Their sale and use to laymen should be discouraged. These are purchased for the most part because of a large volume of over-enthusiastic advertising which suggests to the public the necessity of using these lamps if health and happiness are to be retained, regardless of age or present physical condition of the purchaser. These lamps, for the most part, emit too little ultraviolet to be of any benefit. If they do emit a reasonable amount of ultraviolet and are used with considerable frequency, they will in all probability, according to the advice of some of our best dermatologists, exert an aging effect upon the skin not immediately noticeable. As a matter of fact, very few persons really need frequent tonic treatments and when so needed, they should be under the direction of a physician who knows at least something of the possibilities for good or ill of these lamps. Ultraviolet treatment in general should be expected to be given in an office or hospital and for a relatively small number of pathological conditions.

(7.) Because the sun is the natural source and generator of life on this planet, it would not seem amiss to consider the possibility of its use as highly valuable in the treatment of many pathological conditions. This as we have seen has been done through the ages. At the present time Bernhard and Rollier in the Swiss Alps and others in various parts of the world are using heliotherapy to obtain extraordinary results especially in superficial infections, extrapulmonary tuberculosis, etc. Its one defect lies in its frequent inaccessibility when and where it is needed.

USES

From our past experience and present knowledge it would seem that the proper uses for the three ranges of lamps are as follows:

(a) Lamps producing ultraviolet rays may best be used for certain changes in blood chemistry, hormone activity and treatment of some skin conditions.

The value of the ultraviolet lamps has been much over-rated in the past. The pendulum is now swinging back to normal. A variety of conditions which a few years ago supposed to be best treated by ultraviolet radiations are now much more successfully treated by other means. Then, also, because these lamps emit much of their radiations in the visible and infra-red regions, it is difficult to know just how much credit should be given the ultraviolet rays for some of the successful results attributed to them.

(b) The incandescent tungsten filament lamps and carbon arc lamps with their long range of wave-lengths closely resemble the sun's spectrum. With these lamps heat is produced, penetration assured and possibly some change in body chemistry as well. Such lamps may well be used instead of diathermy for heating the tissues in certain of the superficial conditions. The incandescent lamps also make a most excellent preparation for other forms of treatment (massage, diathermy and galvanism).

(c) The infra-red unit is adapted for use when a rapid hyperemia is desired and penetration is not important. It is best adapted for heating the skin in preparation for diathermy or galvanism and wherever counterirritant effect is desired.

There are two accomplishments solely due to the ultraviolet rays that can be definitely proved: erythema and cure of rickets. These rays, however, may play an important rôle in relieving pathological conditions. For example: Erysipelas may be terminated more quickly, a variety of skin conditions may be helped greatly and the irritation of eczema may often be relieved by radiation with an ultraviolet generator. Whether these, and results similar, are caused entirely by ultraviolet rays, or by their combinations with others, is still an unsolved problem.

It is well known that much more severe sunburn is experienced by exposure on a hazy day than on a clear one.

Physicists tell us that a centimeter of water will eliminate all infra-red rays beyond 14,000 A. What actually happens is that on a bright summer day, if exposed to the sun's rays long enough, we experience both heat and sunburn. On a hazy day, with the same exposure, we feel cooler, but experience a more severe sunburn. A distinct portion of the infra-red rays has been obliterated by the moisture in the air with the result that ultraviolet rays have been able to proceed, with lessened restriction,

to incite a more severe erythema. This illustrates the antithesis between ultraviolet and infra-red, a condition which very possibly obtains between other portions of the spectrum suggesting that in all probability, the sun, or a near equivalent, in which we obtain an interrelation of the three portions of the spectrum, is our best source for general work in phototherapy.

Rollier, a world authority on phototherapy, who has cured by this method thousands of chronic cases of bone and joint diseases during the past thirty or more years, says "I have always insisted on the complete solar spectrum as a therapeutic entity."

Research workers in some of our best technical schools and many physicians in the larger clinics are also in agreement with this sentiment.

For some patients there will still be a definite need for a stronger ultraviolet generator for use in a few, but none the less important, pathological conditions which at present improve best by that treatment. And when rapid hyperemia or "counterirritation" is desired, the infra-red generator may still be an important piece of apparatus in the office equipment.

It is earnestly hoped that in the near future it may be possible to obtain a relatively ideal therapeutic lamp. Such a lamp might best be a bulb type with controlled energy and spectrum output producing approximately the sun's spectrum. A bulb lamp is more conveniently handled than a carbon arc lamp. With an appropriate glass bulb, ultraviolet rays produced by heating the tungsten or other filament will be emitted. A patient will then get the long ultraviolet rays, visible, all the penetrating and possibly some of the superficial infra-red rays. Such a lamp would then be used in whatever conditions the sun's rays would be beneficial, from a mild ultraviolet radiation to intense heat.

CLINICAL FINDINGS

At present, phototherapy emerging from a most unsettled past is still struggling over many problems in common with other branches of therapy. Although much of definite value has been proved recently, in the physics of light by workers in this and other countries, comparatively few of the difficult clinical problems have been solved. There are a variety of factors responsible for these many unsolved chemical problems. Investigators in different laboratories work under varying conditions of climate, light source and dosage. Then too, different investigators work on different types of animals and on healthy human beings, when in reality the apparatus is to be used on pathological tissues in sick human beings. Obviously their skin and body mechanisms are entirely different from those of the sick patient. Then again, much of the benefit of phototherapy undoubtedly depends upon its effects caused by intricate chemical reactions on body tissues and probably also by the stimulation of hormones. Such combinations offer problems which are highly involved and not readily solved.

With the advent of ultraviolet generators, it was hoped that at last we had something specific and practical which would be of vital help to nature in overcoming many of our pathological conditions, especially those of infections. But with more than a decade of sincere work by clinicians and the more scientifically accurate work carried on by laboratory workers, we are compelled to acknowledge its disappointing limitations.

There is still much doubt as to the relative importance of phototherapy in many pathological conditions. On the other hand, there are many cases where this form of treatment, often best followed by massage, can be of very distinct value.

Blood

One of the most difficult problems upon which investigators have been working, is the effect of phototherapy on the blood. Such work is fundamental and of great importance. The results are frequently confusing if not misleading. Many and varied reports of workers often give equally varied conclusions as to the efficacy of the different types of light on the human blood.

The following is a conservative estimate of its value as we know it:

Apparently little or no increase is to be expected in the hemoglobin content and number of red cells in normal individuals. Some cases of secondary anemia are brought up to approach normal but rarely ever beyond, regardless of the number of treatments.

It is admitted by most workers that pernicious anemia is rarely benefited to any appreciable extent by radiation, except that the blood is less toxic. This is probably due in no small measure to the complexity of this condition, as suggested by Dr. W. B. Castle, who states that these cases appear under various disguises and usually show failure in physiological function or deficiency in diet factors. The Taft Heliotherapy Ward of the Cincinnati General Hospital, however, established an enviable record in the treatment of pernicious anemia by heliotherapy before the use of liver therapy was begun. A recent communication from the superintendent states that they feel the combined treatment of heliotherapy and liver to be much more efficacious than liver alone.

According to Friedlander and Wiedmer (1929) the reticulocytes in healthy persons increase during the spring months as contrasted with the winter and they suggest the cause of this increase to lie in the increasing ultraviolet radiation from the sun as it again nears our part of the earth. Various competent workers

have reported an increase in reticulocytes when artificial rays in the ultraviolet region were used during the winter months when these fall below normal.

It seems probable that a normal erythrocyte count may be slightly raised and a low red count may, in some cases, be raised to normal, by frequent exposures to ultraviolet radiation.

Platelets are rapidly increased to normal and possibly somewhat above normal.

Most workers report a rise in the white count. The actual increase in numbers and relative percentage of lymphocytes and leucocytes vary greatly under different conditions.

The coagulation time of blood is shortened.

The percentage of phagocytes is increased.

It has been found that increased immunity has persisted experimentally in animals for only one or two days following an irradiation.

Laurens writes, "While sunlight and artificial energy baths probably benefit general health there is very little, if any, unequivocal evidence that they influence specific immunity, although it is extensively believed that they increase the general resistance of the body to infection by increasing the bactericidal power of the blood."

Blasi in 1929 found that the opsonic action of the blood serum of children with a positive von Pirquet test after ten ultraviolet irradiations had been given, was more marked than that of children with a negative von Pirquet reaction.

Alkalinity is slightly increased. Mayer attributes this to the action of the red (heat) rays.

Basal metabolism is possibly slightly increased.

Tuberculosis

Most authorities agree that sunlight or artificial radiation is definitely harmful in active cases of pulmonary tuberculosis with a temperature of over 100 degrees. This form of treatment may readily light up a lesion which is tending to become quiescent. Mayer feels still more confident of this if the patient has already failed to respond to a fair trial of the routine rest and hygienic treatment.

Rollier believes that in any disease, as well as in pulmonary tuberculosis, with great weakness, toxemia and hectic fever, the sun bath and artificial light as well, do more harm than good. He also adds the following contraindications for use of the sun, in common with many other investigators, "cardiac insufficiency, valvular disease, advanced myocarditis, arteriosclerosis, nephritis, advanced bilateral renal tuberculosis with threatening uremia, lung cases of the nodular type and those in which exudative manifestations predominate".

There is probably little danger of hemoptysis in pulmonary tuberculous cases from the use of sun or ultraviolet radiation when the treatments are given judiciously if the patient is not in an active stage.

Mayer and others emphasize the possibility of helping with phototherapy the following types of tuberculous cases: pleural and peritoneal of either the superficial and lymph node types. There appears to be general commendation of radiation as a beneficial remedy for laryngeal, bone and joint tuberculosis. General body radiation may be given with sun, carbon or mercury arc lamps. Most workers also add reflected ultraviolet rays to the larynx if that be involved.

Skin Diseases

Some common skin conditions are temporarily and some are permanently relieved. The eczemas, psoriasis and some of the skin poisons can frequently be relieved of their more disagreeable sensations even if the underlying cause must be treated by other methods.

Most dermatologists agree that ultraviolet is occasionally an important help in acne vulgaris, especially in intractable cases.

Comedo and acne papulosa of puberty may be controlled best by suitable topical remedies and ultraviolet radiation or both.

Alopecia areata may be benefited by ultraviolet radiation, but only in amounts producing a decided erythema. Dermatologists, in general, feel that all types of alopecia can be treated as successfully by other methods as with ultraviolet radiation.

Spider nevi can be eradicated with blistering doses of ultraviolet radiation if electrolysis is not desired.

Telangiectasia can be eradicated by ultraviolet radiation.

Lupus vulgaris is best treated by ultraviolet radiation. Success will result but requires much patience and time, sometimes two or three years.

Erysipelas may be rapidly terminated by a relatively few treatments depending upon the severity of the case and the intensity of treatment.

Other Diseases

Certain glandular activities are stimulated by phototherapy such as the parathyroid which in turn causes an increase in the metabolism of phosphorus and calcium, thus aiding in the cure of infantile tetany, and rickets. It is thought by some that many of the results of phototherapy are accomplished by an indirect complicated reaction involving the sympathetic system and the production or activation of hormones.

It is well established that ultraviolet radiation stimulates the organism and the cure of rickets and tetany, but larger doses depress and are actually detrimental. This apparently obtains in the case of immunity and bactericidal reaction of blood. Several laboratory workers

report that rats over-irradiated have consistently gained less than other rats receiving a correct antirachitic dose.

Phototherapy is also used daily in conjunction with a variety of other forms of treatment in many of the more common pathological conditions. Arthritis, when confined to a few joints, may be treated with individual lamps or so-called "bakers". When the condition is generalized, an electric light cabinet or some similar device may be used to advantage as a part of the treatment of this obstinate disease. This will stimulate active hyperemia, bringing about the relaxation of blood vessels, which in turn improves the nutrition and carries away the waste products, thus speeding up the process of repair.

Phototherapy is practically indispensable preceding massage in cases of contusions, sprains, post-fractures and in neuritis, neuralgia and bed sores. It may be of great help in most cases of acute sinusitis, otitis media and suppurative otitis media and mastoiditis after surgical measures have been instituted.

From the foregoing it should be definitely realized that each source of phototherapy has its own particular field of usefulness. This must always be borne in mind by the physician in prescribing for his patient if he desires to render the most efficient treatment.

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DINITROPHENOL DANGEROUS IN "REDUCING" NOSTRUMS

The "reducing racket" has a group of new and dangerous drugs, dinitrophenol and related compounds. Racketeers are selling these drugs in fat reducers in spite of reports of deaths caused by their compounds, says W. G. Campbell, Chief of the Food and Drug Administration. "Reducing agents containing these drugs," says Mr. Campbell, "have sprung up like mushrooms all over the country, and are endangering the lives of patrons. The Federal Food and Drugs Act has no jurisdiction over products of this type, dangerous though they may be. All that the Food and Drug Administration can do is to warn the public that these compounds are dangerous."

"Clinical evidence shows," Mr. Campbell said, "that these drugs act by increasing the metabolic rate. This amounts to a speeding up of the body processes, resulting in a destruction of the tissues, including fat, to provide fuel for the accelerated metabolism. Common symptoms are increased temperature, pulse or respiration, or copious sweating." . . . "In particular," Mr. Campbell warned, "these drugs should not be used by individuals suffering from chronic rheumatism, alcoholism, tuberculosis or diseases of the heart, liver or kidneys, as poisonous and otherwise harmful effects are even more likely to manifest themselves. There is also some evidence that they may cause profound disturbance of the blood-forming organs.

"These drugs, in common with many others, may serve a useful purpose when the dosage is properly adapted to the needs of the individual patient, provided there are no contraindications to their use," he says. Proper dosage and indications for use, however, as well as prompt discovery of toxic effects, can be determined only by a skilled physician. Furthermore, there may be unexpected harmful effects that are not disclosed by the first tests. Such effects can be determined conclusively only after extensive trial and use, in addition to the tests which should in all cases be made before the preparation is offered to the public.—*U. S. Department of Agriculture.*

THE CANCER DEATH RATE

Dr. Hoffman's report in *The Spectator* shows a definite increase in the mortality caused by cancer based on a study covering the periods included from 1906 through 1933. According to the report based on a study of the 32,000,000 inhabitants of 50 American cities, there was a rise in the death rate from 71.6 per 100,000 in 1906 to 124.7 in 1933.

A study of 177 American cities shows that in 1932 the rate was 117.1 and in 1933 it was 118.2.

There is a great difference in cancer death rates in various localities, some showing an excess of 150 per 100,000 and others well below 50 with the suggested explanation for Detroit, for example, where many persons in the younger ages are employed in industry.

According to Hoffman, cancer ranks second among the causes of death in this country exceeded only by diseases of the heart "considered as a group". He does not ascribe the statistical increase as due to more exact diagnoses. If no explanation is forthcoming, the facts seem to warrant the conclusion that the concentration of study on the cancer problem has not been so effective as has been hoped even with the impressive number of cured cases.

CASE RECORDS
of the
MASSACHUSETTS GENERAL HOSPITAL

ANTE MORTEM AND POST MORTEM RECORDS AS USED IN WEEKLY CLINICAL-PATHOLOGIC EXERCISES

EDITED BY RICHARD C. CABOT, M.D.
F. M. PAINTER, A.B., ASSISTANT EDITOR

CASE 20301

PRESENTATION OF CASE

The patient was a thirty-six year old American mechanic. Five months before entry he visited his physician because of profuse sweating, slight cough and fever. His temperature was 101.5°. Examination of the chest was apparently negative. The following day his temperature was 105°. He had a slight cough and complained of tightness over the lower part of the sternum. Two days later his temperature was 103.5°. He coughed much more and had some sputum, not blood tinged. He developed some pain in the chest. A few râles were heard posteriorly in the upper left lobe. He was admitted to a hospital, where examination showed slight dullness of the left lung posteriorly, increased tactile and vocal fremitus and flatness on the left anteriorly. The heart sounds were inaudible. The pulse was regular. The liver was felt two fingerbreadths down and was slightly tender. The white blood cell count was 8,700, with 85 per cent polymorphonuclears. A film of the chest showed marked dilatation of the heart shadow with bulging of the right and left borders. Approximately ten days after admission a pericardial friction rub was heard on the right in the fifth interspace. No pericardial tap was performed. His convalescence was long and slow. His temperature remained slightly elevated. Approximately three months after admission to the hospital mentioned a film of the chest revealed fluid at the right base. About seventy-five cubic centimeters was aspirated. The fluid showed a specific gravity of 1.016 and contained 8250 cells, of which 78 per cent were lymphocytes, 13 per cent polymorphonuclears, and 9 per cent large mononuclears. A guinea pig was inoculated. Six weeks later it was reported as alive. The liver increased in size, reaching four fingerbreadths below the costal margin. He had considerable ascites, but this practically disappeared before his discharge. While at home his activity was very much restricted. Ascites and edema appeared, and three weeks after his discharge he was readmitted to the hospital. He remained there for about three weeks, receiving digitalis and various diuretics. The ascites continued and he was transferred to the Massachusetts General Hospital.

Occupational history. He had been a mechanic in a rubber mill for seven years. He had worked in the soft coal mines of Pennsylvania for four years and in several automobile plants in Detroit for six years. Just previous to admission he worked for a shoe company.

The family history is non-contributory. There was no history of tuberculosis.

Past history. He had had the usual childhood diseases. There was no history of rheumatism or pneumonia. He had had gonorrhea, but denied syphilis.

Physical examination showed a pale, well-nourished man with cold, cyanotic extremities. Examination of the heart showed no visible or palpable impulse. The neck veins were moderately engorged and showed slight pulsation. The left border of dullness was in the fifth interspace 11.0 centimeters from the midsternal line, which was two centimeters outside the midclavicular line. The right border of dullness was 5 centimeters from the midsternal line. The supracardiac dullness measured 5 centimeters. The blood pressure was 106/90. The action was rapid and regular, with a rate of 104. The sounds were somewhat muffled at the apex and of a distant, poor quality. At the base they were louder. In the pulmonic area both first and second sounds were slurred. No murmurs were heard. Examination of the lungs showed impaired resonance on the right posteriorly from the angle of the scapula down. This was associated with diminished breath sounds, tactile fremitus and voice sounds. There were no râles. The abdomen was enlarged and contained considerable fluid. The liver was felt 7 centimeters below the right costal margin in the midclavicular line. The edge was tender. There was slight pitting edema of both lower extremities.

The temperature was 100°. The respirations were 22.

Examination of the urine showed a very slight trace of albumin and an occasional leukocyte. The blood showed a red cell count of 5,300,000, with a hemoglobin of 80 per cent. The white cell count was 12,000, with 85 per cent polymorphonuclears. The serum protein was 7.4 per cent. A liver function test showed 40 per cent retention. The stools were negative.

An electrocardiogram showed normal rhythm, a flat T_1 and inverted T_2 and T_3.

X-ray of the chest showed the right border of the heart obscured by thickened pleura and a small amount of fluid. It also obliterated the outline of the right diaphragm. The measurements of the heart were within normal limits. The mediastinum was markedly increased in width, slightly more on the right. Oblique and lateral views of the chest showed hazy cardiophrenic angles. The pulsations of the heart and mediastinum were weak. There was very

little evidence of an appreciable amount of pericardial effusion.

The ascites increased in amount. Several abdominal paracenteses were done. The fluid was yellowish green in color and showed a specific gravity ranging from 1.010 to 1.016. The cell counts averaged 500 to 600 white blood cells of which approximately 50 per cent were lymphocytes. Other therapeutic procedures consisted of rest in bed, digitalis and diuretics, none of which seemed to alter his course. He ran a low-grade fever, 100° to 101°, during his entire stay. About six weeks after admission a cardiolysis was attempted. The patient died on the operating table.

X-Ray Interpretation

Dr. Aubrey O. Hampton: Here are the shadows we described at the right border of the heart and diaphragm. Here is a dense line which is obviously in the interlobar septum. Here you see the septum between the upper and lower lobes, here between the middle and upper lobes. The septa are quite dense and thick. There are also white lines along the left chest wall. That one is about two millimeters thick. That we interpreted as thickened pleura, because on this side there is no obliteration of the costophrenic angle, and we thought nothing except pleura could be distributed so evenly without obliterating the angle. Here there is no thickening. The picture is that of mild hypertrophy and dilatation of the heart without much evidence of pericardial effusion. The left upper border dips down. The total transverse heart measurement is 14.5, the internal diameter of the chest 30. Over 14 is probably enlarged, but in a chest as large as that we thought the heart measurements within normal limits. The mediastinum is quite wide. The shadow of the aorta on both sides is obscured.

We took both oblique views to demonstrate the sign of pericardial effusion at the cardiophrenic angle, that is, obliteration of the angle. I do not think that sign is worth much when the pleura is thickened. The cardiac pulsations were weak, and yet we could see them. When we can see heart pulsations with the fluoroscope we do not feel like saying that there is an appreciable amount of fluid in the pericardium. Again, here is the thickened pleura along the axillary line.

In this film, taken a month later, there is a marked change in the whole picture. Both diaphragms are now obliterated and we have evidence of fluid in the pleural cavity on the left, perhaps a little more on the right. His mediastinal shadow is also more indistinct. We found no calcium in the pericardium or pleura.

Clinical Discussion

Dr. Paul D. White: This case is one of the failures of treatment in our series of patients with Pick's disease that we have had under our care in the past five years. Of a total of thirteen cases of Pick's disease (constrictive pericarditis), ten have been operated upon and three have not. Of the ten cases operated upon five have been completely relieved of their symptoms and of their signs of Pick's disease, that is, of their dyspnea and of enlargement of the abdomen and ascites, and have returned to practically normal activity. That is a very good batting average of fifty per cent. The case under discussion today was one of three fatal cases. This man died at the time of operation. Two of the three patients who died were the oldest cases of the series of ten. This man was thirty-six, the oldest was fifty-two, and the third was twenty-three. The age undoubtedly enters into the matter of operative risk, but perhaps as important is the question of the activity of the process.

Most of the ten patients who were operated on, and especially those who were relieved, had little evidence of infectious activity, although two of the five successful cases had had recent polyserositis and there was some doubt as to the wisdom of operation at the time because of the possibility of stirring up a fresh infection, tuberculous for example. These two doubtful cases, however, were young and they happened to be one hundred per cent relieved.

The patient under discussion now obviously had an active infection and this infection obviously was polyserositis, including involvement of pleura and of pericardium, as indicated both by history and by examination (physical and x-ray). We did not know the etiology, that is, whether it was tuberculous or not. A certain percentage of the cases of Pick's disease are tuberculous, probably about thirty per cent.

This patient was obviously in distress, and to survive obviously needed surgical relief. The signs were more marked than in any other case we have seen. He had a high degree of paradoxical pulse as important evidence of constriction of the heart. The pulse pressure was only a little over 10 millimeters, the blood pressure being 104 systolic and 90 diastolic. During inspiration the pulse would disappear. It was one of the most marked instances of paradoxical pulse that I have ever encountered in the absence of much effusion into the pericardium.

We decided, in spite of his age and the activity of the infection, that it was fair to take the risk, and we imposed that risk on Dr. Churchill.

Dr. Edward D. Churchill: This case is quite a contrast to the usual case of Pick's disease, in which surgery has been so successful.

At operation the pericardium was exposed and opened. The parietal pericardium was over one centimeter in thickness. The heart was in no place in contact with the parietal pericardium, but was surrounded by a layer of this

straw-colored fluid. When the fluid was removed the heart did not expand to fill the pericardial cavity, being tied down by the inflammatory reaction in the visceral pericardium and by the thickening of the pericardium at the base of the heart where the great vessels enter and leave the pericardium. It was obvious that we were dealing with a condition for which we could do nothing surgically, and also that we were facing an immediate fatality.

In the group of patients suffering from a reduced cardiac inflow, unless conditions can be improved by operation the operation itself is a dangerous procedure. In the first case of this type—we have had two—the pericardium was found studded with tubercles. That man died twelve hours after the operation. In the case of the patient under discussion the same situation was encountered except that there were no obvious tubercles,—the reduction of cardiac inflow was the same. The one hope was to see if the visceral pericardium could be stripped off the heart; but the patient succumbed in the process.

A Physician: How much fluid did this man have?

Dr. Churchill: It could not be measured, but was about 250 or 300 cubic centimeters. The fluid in itself was not the cause of the tamponade, because the filling of the heart was not improved by its removal.

Dr. White: May I ask about two or three of the other cases that were operated on successfully? Is it not true that in some of these you had to take off the visceral as well as the parietal pericardium?

Dr. Churchill: Yes, I think that is true.

Dr. White: In this case the condition was more marked, was it not?

Dr. Churchill: Yes, and more acute. In the other cases, except one I think, there was no fluid between the two layers.

Dr. White: In some of the other cases when you took off the parietal pericardium the heart was able to expand at once, was it not? There was much less thickening of the visceral pericardium in them. There were other cases in which the constriction was due to involvement of both parietal pericardium and visceral pericardium.

Dr. Churchill: We found one case in which there was encapsulated fluid over the right auricle. Here both layers of pericardium were resected in order to allow normal expansion of the auricle.

Dr. White: Although that case had some fluid in the pericardium, there was a complete recovery.

Dr. Churchill: Yes. But the tissue was different. It was organized fibrous tissue, whereas in to-day's case the pericardium was an acute inflammatory edematous tissue.

Dr. White: One further important observation about the third case that died, the older patient, fifty-two years old, is that after pericardial resection from the right heart chambers pulmonary edema developed, and death ensued in a few days, apparently from pulmonary congestion, the result of release of the right ventricle, with the left ventricle still bound in adhesions.

Dr. Churchill: In that case also we misjudged the condition of the liver. I think the extreme degree of cirrhosis of the liver shown at autopsy may have played a part.

Dr. George W. Holmes: Would a pneumopericardium allow you to distinguish between the two types of cases, the one that is successful and the one that is not?

Dr. Churchill: If we had taken out the fluid and replaced it with air it might.

Dr. White: It would be very difficult.

Postoperative Pathologic Diagnosis

Tuberculous pericarditis, acute and chronic.

Pathologic Discussion

Dr. Tracy B. Mallory: We did not have what a pathologist would consider a postmortem examination. In fact all that was possible after the patient's death was to continue the exploration a little in the operative field, which Dr. Churchill did and allowed me to observe. Neither of us thought that the pericardium looked like a tuberculous one at the time of operation. It was tremendously thickened, but nothing that we could see in gross suggested any miliary lesions or tubercles. There was no definite calcification. The pericardial sac, besides the fluid, contained extraordinary amounts of spongy fibrin. The layer of gelatinous material in which were small collections of fluid was as I remember it everywhere 1.5 centimeters or thicker, but I think a good deal of the exudate was almost more solid than fluid. Both the visceral and the parietal pericardium were markedly thickened and the inflammatory infiltration extended down through the diaphragm as well. Because of the uncertainty as to the etiology at the time of operation, considerable amounts of fluid were removed and cultured. In the Surgical Research Laboratory an anaerobic streptococcus was grown from the material. Meanwhile we were putting through sections and we found tuberculosis, but we were unable to demonstrate tubercle bacilli with stains. Some of the fluid had been put into a monkey's pericardium by Dr. Churchill. He has brought this specimen over. As you see, it is a beautiful tuberculous pericardium, and the omentum is studded with tubercles. This has not been sectioned as yet, but from the appearance of these lesions I do not believe there is any doubt as to the tuberculous character.

I will take a moment to show you some sections.

DR. CHURCHILL: This monkey lived for a month and then was quite sick. He was chloroformed and an autopsy performed a week ago. At the time of his death he showed marked edema of the scrotum, hands, and eyelids. He had 150 cubic centimeters of straw-colored fluid in the belly, 25 cubic centimeters in the right pleural cavity. In other words he died with the clinical picture that this patient had, partly tuberculosis and partly cardiac failure.

DR. MALLORY: This first section is from one of the spongy masses of fibrin scraped out of the pericardial cavity. It contains no collections of mononuclears, nothing that suggests tubercle formation. Sections at the fibrous pericardial wall, however, such as this second one, show as typical miliary tubercles as one could ask for.

DR. RICHARD C. CABOT: Would you make a diagnosis on this if you had not employed the monkey test?

DR. MALLORY: I felt pretty sure of it, in spite of not being able to demonstrate tubercle bacilli. I do not think a negative acid-fast stain means very much. If we had cut one hundred sections and looked at each for an hour and then not found tubercle bacilli it would mean something. Short of that it hardly does.

DR. CHURCHILL: I think the one interesting thing that it brings out is how easy it is to be misled by obtaining cultures of anaerobic streptococci. Two of the four tubes in which the pericardial exudate was planted grew a short chained anaerobic streptococcus. The monkey showed a classical case of tuberculosis.

CASE 20302

PRESENTATION OF CASE

First admission. A forty-one year old English seamstress entered twenty-one years before her final admission complaining of abdominal pain.

Two weeks before entry she began to have a dull constant pain in the epigastrium and the left upper quadrant passing along the left of the sternum. This was accompanied by a great deal of belching. Since that time she had had a similar pain occurring two or three hours after meals and lasting three or four hours. There was no vomiting until two nights before entry, when she brought up about a cupful of blood. The pain was somewhat relieved by soda. There were no tarry stools or jaundice.

She was discharged against advice before x-ray films could be taken.

History of interval. She was perfectly well after her discharge except for occasional attacks of belching. Nine years after her discharge she was in bed for eight weeks, during which time she vomited two or three times a day. There was some abdominal pain which was at times very severe and cramp-like but not related to meals. Two or three times a year she had attacks of pain in the "pit of her stomach" which doubled her up. The attacks would start with nausea and vomiting, followed by pain. Two weeks before her second admission she had diarrhea which lasted several days. During the past ten years she had had typical anginoid attacks of precordial pain with radiation down the left arm. The attacks often came while she was recumbent, several times during the day and night. These attacks were relieved by nitroglycerin.

Second admission, thirteen years after her previous discharge. She entered this time for excision of a fistula in ano.

Physical examination showed an ischiorectal abscess on the right. The chest was negative. The heart sounds were of poor quality. There were no murmurs. There was tenderness on pressure over the third and fourth ribs in the precordial region. The blood pressure was 215/115. Examination of the abdomen showed tenderness on pressure over the right lower quadrant with a question of slight spasm. There was costovertebral tenderness, definite on the right and slight on the left.

X-ray examination of the whole gastrointestinal tract showed no evidence of organic disease.

The fistula in ano was excised. She continued to have anginal attacks, about two or three a day. A cardiac consultant suggested cervical sympathectomy.

She was discharged at the end of three weeks.

Three years and a half later she gave a history of having had for the past five years sudden fainting spells during which she would lose consciousness and frequently hurt herself in falling. These attacks came on more frequently before her third admission and made it impossible for her to go out of doors alone or do any cooking. During this period she had increased frequency and nocturia up to three times a night. She also had chronic cough with purulent sputum. During the six months before her third admission she had severe frontal headaches and on occasions tinnitus. She had lost about eight pounds during the year before admission.

Third admission, three years and seven months after her previous discharge.

Physical examination showed an obese, pale woman. The heart was not enlarged. The supracardiac dullness measured 6 centimeters. There was a rough systolic murmur at the base which was also audible at the apex. The aortic second sound was loud and snapping. There was an unusual degree of precordial hyperesthesia to percussion. The left border of dullness was not made out. The blood pressure was 198/114. There was marked peripheral arterio-

sclerosis. The abdomen was obese. The liver edge was not felt. There was a mild degree of pitting edema over the shins.

X-ray examination of the heart showed it to be slightly enlarged in the region of the left ventricle.

The temperature was 98°, the pulse 90, the respiration 22.

Examination of the urine showed a specific gravity of 1.025 and a brown test for sugar. The sediment showed an occasional epithelial cell. Examination of the blood showed a red cell count of 4,400,000 with a hemoglobin of 70 per cent and a white cell count of 10,350, with 70 per cent polymorphonuclears. The stools were negative, except that one out of five examined showed a positive guaiac. A Wassermann test was negative. The blood sugar ranged from 175 to 210 milligrams.

An electrocardiogram showed normal rhythm, rate 80, and left axis deviation. T_3 was flat.

Her anginal attacks were controlled by nitroglycerin. She was digitalized and her mild diabetes was treated by regulation of her diet. She refused to have alcohol injections and was discharged at the end of six weeks.

History of interval. After her discharge she continued to have anginal attacks with occasional fainting spells. Three months before her fourth admission, two years and a half later, she began to have sharp twisting pains which lasted for two or three minutes and occurred every two or three days. The pain was located in the left lower quadrant and was very intense. On the day before admission during one of these attacks she had an attack of diarrhea and passed approximately two quarts of blood. She had always been more or less constipated, requiring cathartics. The fistula in ano repair had been unsuccessful and she always experienced pain during defecation.

Fourth admission. Physical examination was practically the same as on her third entry. The blood pressure was 190/100.

The temperature was 99°, the pulse 85. The respirations were 20.

Examination of the urine showed a specific gravity of 1.020, a slight trace of albumin and a red test for sugar. Examination of the stools showed a four plus guaiac.

A barium enema showed a diverticulitis of the sigmoid and a spastic cecum. There was no organic pathology in the esophagus, stomach or duodenum.

A proctoscopic examination showed the rectum full of clotted blood, but no abnormalities or obstruction were observed. She was discharged on the twelfth day.

History of interval. Three weeks before her fifth admission, a year and eight months later, she was suddenly seized with severe cramp-like pain over the entire abdomen. This was accompanied by anorexia, which persisted. Further description of the pain was impossible to obtain. Two weeks before entry her bowels suddenly stopped moving. There was nothing abnormal about her bowel habits or the appearance of the stools just prior to this incident. Two days before admission she began to have persistent vomiting.

Fifth admission, a year and eight months after her fourth discharge.

The patient was in a semicomatose condition and was very uncoöperative. Physical examination done in the ward the morning following admission showed an elderly woman lying in bed complaining of abdominal pain which could not be localized. During the examination she began to retch and raise a small amount of mucus, although she strained vigorously. Suddenly her respirations became labored. Her precordium was very tender and no heart sounds were audible.

The temperature was 100.5°, the pulse 96, the respiration 23.

Examination of the urine showed a large trace of albumin, a green test for sugar and large numbers of white blood cells. The blood showed a white cell count of 12,600. The non-protein nitrogen was 53 milligrams.

Differential Diagnosis

Dr. William D. Smith: I am going to be rather sketchy in this discussion for more than one reason. In the first place she had five admissions, and to take them all up one would have to talk all the afternoon. In the second place I cannot make a diagnosis.

She came in first when she was forty-one years old with a history of two weeks' epigastric and left upper quadrant pain which radiated along the left border of the sternum and was accompanied by a large amount of belching. Two days before entry she vomited a cupful of blood. In addition to the three usual causes of vomiting blood and in addition to the unusual ones, such as polyp and benign tumors, the belching and pain radiating up the left sternal border would almost make me want to include diaphragmatic hernia or possibly a peptic ulcer of the lower end of the esophagus. However, we have absolutely nothing by which we can make a diagnosis by exclusion. Possibly the fact that she vomited blood once and then lived twenty-one years makes an ulcer that healed the best possibility.

She came in again at the age of fifty-four on account of a fistula in ano. We will disregard the fistula.

We are told that nine years after the first attack of epigastric distress she was in bed for eight weeks, during which time she vomited two or three times a day and had abdominal pain which was very severe and cramp-like and not related to meals. In addition to the abdominal pain she had attacks of pain in the pit of the stomach which doubled her up. The

attacks started with nausea and vomiting and then the pain followed. One thinks of possible gall bladder, or of recurrence of an ulcer. There is no point in thinking of all the possible causes and then trying to exclude them, because there is no evidence by which you can exclude and then make any diagnosis.

Here is another interesting point. During the past ten years, from the age of forty-four, she had had typical anginal attacks of precordial pain with radiation down the left arm, occurring while she was recumbent during the day or night and relieved by nitroglycerin. If there was any relation between that anginoid pain and the upper abdominal discomfort I should think again quite seriously of diaphragmatic hernia, that is, the type of diaphragmatic hernia in which Dr. Bock has been interested. Upper abdominal pain associated with anginal pain. Some of these cases are actually diagnosed angina pectoris. They are difficult to find by x-ray. They are precipitated by increased abdominal pressure. If there is increased abdominal pressure, a bit of the stomach gets pushed up through a ring and you may get very definite anginoid symptoms which radiate down the left arm.

Physical examination does not help much. She had a blood pressure of 215/115. The abdomen showed slight tenderness on pressure over the right lower quadrant with questionable slight spasm. If any one wishes to consider chronic appendicitis he is welcome to do so. I am not interested. Furthermore we have thrown in for good measure the fact that there was costovertebral tenderness, definite on the right and slight on the left. I am going to disregard that too.

X-ray of the whole gastro-intestinal tract was negative. That is not very helpful.

She was discharged and did not appear again until she was fifty-seven years old. At that age she had a new symptom, sudden attacks of fainting during which she lost consciousness frequently, falling down and hurting herself. My first thought in view of the hypertensive heart, angina, and presumable coronary sclerosis is that very likely these were Stokes-Adams' syndromes. That is excluded later, because she had a perfectly normal electrocardiogram. There was no evidence of partial block or anything else of significance.

My next thought was, did she have hemorrhage? Did she bleed and lose consciousness? That is not very good either, because a person does not as a rule suddenly lose consciousness and fall down.

My next thought was cerebral arteriosclerosis. Are the fainting attacks cerebral episodes? That is pretty hard to say, because there are no other evidences of cerebral arteriosclerosis such as attacks of aphasia or transient paralyses or vertigo. Here again we might consider all the causes of sudden loss of consciousness and try to make a diagnosis by exclusion, but we have absolutely no evidence by which to exclude, so far as I can see. It may be cerebral arteriosclerosis.

The attacks came on more frequently and made it impossible for her to go out-of-doors or do cooking. She had increased frequency and nocturia. She may be getting vascular nephritis secondary to her essential hypertension. She also had chronic cough and purulent sputum.

During the past six months she had severe frontal headaches and occasional ringing in the ears. There again we might say anemia from blood loss. We might say cerebral arteriosclerosis. I say cerebral arteriosclerosis rather than high blood pressure, because I am one of the iconoclasts who do not believe that hypertension in itself gives symptoms. I believe the cerebral vessels, the kidneys or the heart are responsible for the actual symptoms. I do not believe we get symptoms due solely to the high blood pressure.

She lost eight pounds during the past year; not a very big percentage in an obese woman.

We have another physical examination in which we are told that she was obese and pale, and that the heart was not enlarged. The supracardiac dullness was 6 centimeters. There was a rough systolic murmur and the aortic second sound was loud and snapping. That rules out another cause of fainting. It occurred to me that she might have aortic stenosis and the fainting was cerebral anemia; but with a loud aortic second she probably has not aortic stenosis. People do not faint just because they have heart disease, and there is nothing to suggest any other sign of aortic stenosis except the rough systolic murmur. There was an unusual degree of pericardial hyperesthesia on percussion. That may have been the hyperesthesia that is sometimes associated with angina. On the other hand it is not at all uncommon to find paresthesia of the left chest, tender spots, nerve endings in the skin with people who have no heart disease. I cannot draw any conclusion from that.

The blood pressure is still high, 198/114. The abdomen is obese. The liver is not felt. There is a slight degree of pitting edema over the shins.

X-ray examination of the heart showed it to be slightly enlarged in the region of the left ventricle. Certainly with that blood pressure it ought to be big.

The examination of the urine shows diabetes, but what of it? The blood showed a mild secondary anemia, I do not know why. She may have malignancy.

The electrocardiogram does not help.

The angina attacks were controlled by nitroglycerin. She was digitalized and the mild dia-

betes treated. She refused alcohol injections.

I should like to comment on that angina, because it is a little unusual. Here is a woman who begins to have angina pectoris at forty-four. She has angina attacks for eighteen years before she dies, attack after attack. She has angina from the time she is forty-four until she is sixty-two. She is having attacks when quiet day or night. It is very extraordinary. I think Dr. Sprague might agree that it is extraordinary that she has angina decubitus and lives as long as that.

When she comes in for the fourth time she is sixty years old. Since the last discharge she had continued to have angina and attacks of fainting.

I do not feel very well qualified to discuss that huge rectal bleeding. I have never seen a diverticulitis with bleeding like that, and I do not believe that it occurs. One wonders whether she could have had any such bleeding from hemorrhoids. She had been examined rectally for her fistula; I think hemorrhoids that would have bled like that must have been noted. Furthermore I am not at all sure that the bleeding from hemorrhoids would leave a rectum full of clotted blood. I think bleeding as near the anal orifice as that would be evacuated. I should doubt if it would leave a rectum full of clotted blood. Could she have had a bleeding ulcer all these years and a new ulcer? It is unlikely. Then one thinks of polyps. Could the first bleeding at forty-one have been due to polyp? That does not seem reasonable to me. Has she malignant disease? Cancer is the most common cause of intestinal bleeding. There is no answer by x-ray, no answer by proctoscopy. If she had malignancy on the right side on the ascending colon she certainly ought to have been more anemic.

Now this terminal event preceding her fifth and final admission. She had pain two weeks before she came in. Her bowels suddenly stopped moving. Two days before she came in she started to vomit. She came in obviously in a very serious condition. Of course one thinks about obstruction. She could not have had a high obstruction without being sicker than that in forty-eight hours. Furthermore if she had had a high obstruction she would have had a high non-protein nitrogen, more than 53. Could she have had a low obstruction? partial obstruction which became complete, with resulting toxemia and perhaps peritonitis? We have no examination of the abdomen here. We do not know whether it was tender,—nothing except that she had pain which she could not localize.

I feel quite hopeless. Of course there are certain things that she obviously had. She had hypertensive and arteriosclerotic heart disease with coronary involvement, general arteriosclerosis, and cerebral arteriosclerosis. She probably had some arteriolar sclerosis of the kidneys, but not to such a extent that we can call it a nephritis. She had a mild diabetes. In the last entry she had a great many white blood cells and albumin, and apparently has developed a urinary infection. That is all easy. I cannot link up her vomiting of blood at forty-one with her massive hemorrhage at sixty and death at sixty-two. Polyp which became malignancy is one thought. I do not believe it is a good one. She is sixty odd years old. She has had hemorrhage. She is in the cancer age. Malignancy is the most common cause of bleeding in the intestinal tract. My guess is that she had malignant disease of the gastro-intestinal tract, probably of the large intestine.

Another question which I cannot decide is whether she died suddenly as the result of obstruction toxemia and peritonitis or whether the terminal event may have been due to pulmonary embolus or coronary thrombosis. I certainly cannot tell that on any evidence that is given.

Clinical Diagnosis

Subacute intestinal obstruction.

Anatomic Diagnoses

Coronary thrombosis.
Infarct of the heart with rupture.
Hemopericardium.
Arteriosclerosis, coronary, cerebral and aortic, marked.
Cholelithiasis.
Cholecystitis, chronic.
Diverticulosis of the descending colon and sigmoid.
Chronic vascular nephritis.
Infarcts of lenticular nuclei.

Pathologic Discussion

Dr. Benjamin Castleman: We cannot account for the bleeding in the gastro-intestinal tract. All we found were numerous diverticula in the sigmoid and descending colon, as was shown by the x-ray film taken at one of her admissions. There was no evidence of infection or bleeding at that time; no signs of ulceration or tumor in the whole gastro-intestinal tract.

The immediate cause of death was coronary thrombosis with infarction of the heart and rupture causing a hemopericardium. Apparently this is one of the cases of angina and coronary disease that produce abdominal symptoms that Dr. Levine reported in 1918.

Do you agree with that, Dr. Sprague?

Dr. Howard B. Sprague: Yes.

I should like to add to what Dr. Smith said that it is a very unusual story for a woman to have angina beginning at this age and continuing for ten years with repeated attacks. It is very disturbing to find that it can occur, because one not infrequently has such a problem in a differential diagnosis and seeing a woman with this vague distress in the chest one usually guesses that it is not angina. Apparently there can be a very severe progressive coronary disease present with such a history.

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LAW LEADS THE WAY

THE news of the raising of the standards for entrance to the practice of law in Massachusetts comes as the east wind in Boston on some almost intolerably hot and sultry day. The Supreme Court has taken action to remedy a situation which has called for years for improvement, and in establishing reasonably high regulatory standards has begun a needed housecleaning.

Massachusetts has educational institutions which are known all over the world and of which the citizens may well be proud. These schools, whether secondary, university, college or institute have set high standards of achievement and are recognized leaders in education. It is important, however, to point out that side by side with these schools of distinction the Commonwealth has encouraged by the laxity of its regulatory procedures, professional schools "of the baser sort".

Contrasted with the refreshing breeze from the Bench, is the unsavory atmosphere in which the legislature has just been prorogued. The General Court in its last session as it has done for many years refused to raise the statutory standards for the education of practitioners of medicine in Massachusetts. It has been reported that the standards for admission to the Bar in Massachusetts were lower even than for admission to the practice of medicine. Certainly medicine now lags far behind. Why should there not be required for medicine at least two years of work in an approved college and then a medical course in an approved school? The standards for the practice of medicine should be at least as high as for the practice of law in Massachusetts, and it is not too much to ask that they should be as high in Massachusetts as the general level of the other states.

Massachusetts has become a laughing stock among the states for its medical practice act. The legislature will change the law as soon as public opinion demands it. It is the duty of every physician to enlighten public opinion and to stimulate it to action. The health of the people of the Commonwealth is at stake.

THE COMMONHEALTH, VOLUME 21, NO. 1

The Commonhealth, the bulletin of the Massachusetts Department of Public Health, has devoted its issue for the first quarter of 1934 to a discussion of adult hygiene. In this symposium the following topics have been ably presented by their authors: The Care of the Skin, by William J. Macdonald, M.D.; Nerves, by Abraham Myerson, M.D.; Heart Disease, by Samuel H. Proger, M.D.; Can High Blood Pressure Be Avoided? by Lawrence B. Ellis, M.D.; Arteriosclerosis, by Paul D. White, M.D.; The Truth About Bright's Disease, by James P. O'Hare, M.D.; The Cancer Problem, by Ernest M. Daland, M.D.; What The Public Should Know of Diabetes, by Elliott P. Joslin, M.D.; Arthritis, by Robert B. Osgood, M.D.; Chronic Rheumatism, by Eleanor J. Macdonald, A.B.; The Effects of Fatigue, by John H. Talbott, M.D.; Pyorrhea, by E. Melville Quinby, D.M.D.; Why Gums Bleed, prepared by the Massachusetts Dental Hygiene Council, and Hemorrhoids, by L. S. McKittrick, M.D.

The list of subjects shows how comprehensively the discussion has been covered, and the whole bulletin is added evidence to the interest that is being taken in driving home to the lay public the importance of preventive medicine. The article, What Price Health? contributed by Dr. Mary R. Lakeman, Supervisor of Education in the Division of Adult Hygiene is of particular value, comprising, as it does, a personal health score card of thirty-seven points, that can be kept by the individual from month to month.

The bulletin concludes with an article on diet, and an evaluation of the importance of the radio in public health education, by Dr. Herbert L. Lombard, Director of the Division of Adult Hygiene.

THIS WEEK'S ISSUE

CONTAINS articles by the following named authors:

RECTOR, JOHN M. A.B., M.D. University of Pennsylvania School of Medicine 1930. Formerly Assistant Resident in Pediatrics, Children's Hospital, Boston. Address: Medical Arts Building, 2000 Van Ness Avenue, San Francisco, California. Associated with him is

WHEELER, WARREN E. S.B., M.D. Harvard University Medical School 1933. Formerly Resident in Bacteriology, Children's Hospital, Boston. Address: Massachusetts General Hospital, Boston, Massachusetts. Their subject is "The Use of the Ketogenic Diet in Chronic Pyuria." Page 143.

SMITH, CLEMENT A. A.B., M.D. University of Michigan Medical School 1928. Junior Assistant Physician, Children's Hospital, Boston. His subject is "The Clinical Basis and Present Status of Vaccination Against Tuberculosis." Page 147. Address: 319 Longwood Avenue, Boston, Massachusetts.

FARBER, SIDNEY. B.S., M.D. Harvard University Medical School 1927. Instructor in Pathology, Harvard Medical School. Pathologist, Boston Children's Hospital. His subject is "Fulminating Streptococcus Infections in Infancy As a Cause of Sudden Death." Page 154. Address: 300 Longwood Avenue, Boston, Massachusetts.

GREEN, WILLIAM T. A.B., A.M., M.D. Indiana University School of Medicine 1925. Instructor in Orthopedic Surgery, Harvard Medical School. Junior Assistant Orthopedic Surgeon, Children's Hospital, Boston, and Peter Bent Brigham Hospital, Boston. His subject is "Pyogenic Infections of Bones and Joints in Infancy." Page 159. Address: 300 Longwood Avenue, Boston, Massachusetts.

GALLISON, DAVIS T. Ph.B., M.D. Tufts College Medical School 1924. Junior Visiting Physician, Boston City Hospital. Instructor in Medicine, Tufts College Medical School. His subject is "Gastro-Intestinal Allergy as a Cause of Intestinal Obstruction." Page 164. Address: 520 Commonwealth Avenue, Boston, Massachusetts.

HOFFMAN, FREDERICK L. LL.D., Consulting Statistician Prudential Insurance Company. Member of Board of Directors of the American Society for the Control of Cancer. In charge of Cancer Statistics Library, Cancer Laboratory of the University of Pennsylvania. Member of American Cancer Research Association. Honorary Member, German Cancer Research Society. His subject is "Cancer of the Pancreas." Page 165. Address: 133 South 36th Street, Philadelphia, Pennsylvania.

COTTON, FREDERIC JAY M.D., AND MORRISON, GORDON MACKAY, M.D. See page 817, issue of April 12 for records of authors. Their subject is "Resection of the Lower End of the Ulna (Subperiosteal)." Page 170.

LOWRY, FRANKLIN P. B.S., M.D. Harvard University Medical School 1916. Chief of Department of Physical Therapy at the Newton Hospital. Instructor in Electrotherapy at the Sargent School of Boston University. Member of special committee on Post-Graduate Education in Physical Therapy appointed by the Council of Physical Therapy of the American Medical Association. His subject is "Some Present-Day Conceptions of Phototherapy." Page 171. Address: 313 Washington Street, Newton, Massachusetts.

CORRESPONDENCE

REVOCATION OF THE REGISTRATION OF DR. VAN GAASBEEK

Board of Registration in Medicine
State House, Boston

July 19, 1934.

New England Journal of Medicine,

This is to inform you that at a meeting of the Board of Registration in Medicine, held July 12, 1934, it was voted that the license of Dr. Harold Van Gaasbeek, 167 Broadway, Chicopee Falls, Massachusetts, be revoked, because of his conviction in court as an accessory before and after the fact (abortion).

Very truly yours,
STEPHEN RUSHMORE, M.D., *Secretary.*

OFFICERS ELECTED BY THE BOARD OF REGISTRATION IN MEDICINE

Board of Registration in Medicine
State House, Boston

July 16, 1934.

New England Journal of Medicine,

This is to inform you that at the annual meeting of the Board of Registration in Medicine, held July 12, 1934, Dr. Charles P. Sylvester, of Boston, was elected Chairman, and Dr. Stephen Rushmore, of Boston, was elected Secretary for the ensuing year.

Dr. Edward A. Knowlton, of Holyoke, was designated to act with the Chairman and the Secretary in the Department of Chiropody.

Very truly yours,
STEPHEN RUSHMORE, M.D., *Secretary.*

RECENT DEATHS

McCRILLIS—MARY F. MCCRILLIS, M.D., of 6 Pleasant Street, Somerville, Massachusetts, died in the

Glenside Sanitarium, Jamaica Plain, July 20, 1934, after a long illness.

Dr. McCrillis was born in 1856 and graduated from the Boston University School of Medicine in 1882. She practiced in Chicago until 1918 when she came east and settled in Somerville.

She had been identified with the work of the Red Cross.

A brother, Alonzo McCrillis, of Sandwich, New Hampshire, survives her.

HERRIN—HERBERT E. HERRIN, M.D., of 400 Walk Hill Street, Mattapan (Boston), died July 16, 1934, on the steamer Somerset en route from Miami to Baltimore.

He was born in 1883 and graduated in medicine from Tufts College Medical School in 1910. He joined the Massachusetts Medical Society in 1923.

He held the position of Assistant Superintendent at the Boston State Hospital after services at the Bangor, Maine, State Hospital and the New Hampshire State Hospital at Concord.

He was a member of the Massachusetts Psychiatric Society, the New England Society of Psychiatry, a Fellow of the American Psychiatric Society and a member of the Masonic order.

NOTICE

CORRECTION

In the issue of July 12, page 94, the *Journal* incorrectly stated that "Acute Intestinal Obstruction" by Monroe A. McIver was published by the Harvard University Press. This should have read: New York: Paul B. Hoeber, Inc. $7.50.

NOTICE OF MEETING

THE MIDDLESEX SOUTH DISTRICT MEDICAL SOCIETY AND THE MIDDLESEX SOUTH DISTRICT MEDICAL GOLF ASSOCIATION

will hold a joint meeting on Wednesday, August 1, 1934, at the Woodland Golf Club, Washington Street, Auburndale.

PROGRAM

Luncheon. 12 noon.

After the luncheon a business meeting will be held. The Norfolk District Medical Society has requested this Society to coöperate in the correction of the unfair competition of the municipal and endowed charitable hospitals, with private physicians. Resolutions accepted by the Norfolk District Society were printed in the *New England Journal of Medicine*, page 1235, June 7, 1934 issue. Action will be taken on this matter.

The guest speaker will be Captain Charles J. Van Amburg, a leading authority on Ballistics and a member of the Massachusetts Department of Public Safety. His topic will be "Ballistic Evidence" with lantern slide illustrations.

The Golf Association will hold a meeting. Purpose: Election of Officers.

An invitation is extended to all members to play golf, either in the morning or after the completion of the program. The green fee is $2.00. Prizes will be awarded.

As in the past, members are not assessed for the luncheon. Guest luncheon tickets are eighty-five cents and may be obtained either from Dr. Edward Mellus or the secretary.

The Woodland Golf Club may be reached from Watertown Square by taking Watertown Street, then turning on Washington Street and continuing on it for about one-quarter of a mile beyond Commonwealth Avenue. It is near the Newton Hospital. The telephone number is West Newton 1900.

The Middlesex South District Medical Society: Allen H. Blake, M.D., President; Alexander A. Levi, M.D., Secretary.

The Middlesex South District Medical Golf Association: Norman Hunter, M.D., President; Alexander A. Levi, M.D., Secretary.

SOCIETY MEETINGS, CONGRESSES AND CONFERENCES

August 18 - September 30—Medical Study Trip to Hungary. See page 975, issue of May 10.

September 3-6—American Public Health Association, at Pasadena, California. Dr. J. D. Dunshee, Chairman, Local Committee on Arrangements.

September 4, 5, 6—International Union Against Tuberculosis. For information address the National Tuberculosis Association, 450 Seventh Avenue, New York City.

September 10, 11, 12, and 13—American Congress on Physical Therapy will meet in Philadelphia at the Bellevue Stratford. For details write American Congress of Physical Therapy, 30 North Michigan Avenue, Chicago, Illinois.

September 10-15—First International Congress of Electro-Radio-Biology will be held in the Doges Palace at Venice. For details address the General Secretary of the Congress, Dr. Giocondo Protti, S. Gregorio 173, Venice (Italy).

September 27 and 28—International Association for Preventive Pediatrics will be held at Lyons. For details address the Secretary of the I. A. P. P., 15 rue Lévrier, Geneva (Switzerland).

September 28-29—New England Surgical Society will meet at Burlington, Vermont. For details address the Secretary, Dr. John M. Birnie, 14 Chestnut Street, Springfield, Mass.

October 22 - November 2—1934 Graduate Fortnight of the New York Academy of Medicine. See page 1240, issue of June 7.

October 31 - November 2—Massachusetts State Nurses' Association, Hotel Statler, Boston. For information write Miss Helene G. Lee, R.N., 420 Boylston Street, Boston.

April 29 - May 3, 1935—The American College of Physicians will meet in Philadelphia. For information address Mr. E. R. Loveland, Executive Secretary, 133-135 South 36th Street, Philadelphia, Pa.

June, 1935—Medical Library Association will meet in Rochester, N. Y. For details address the Secretary: Miss Frances N. A. Whitman, Librarian, Harvard University Schools of Medicine and Public Health, Boston, Mass.

DISTRICT MEDICAL SOCIETY

THE MIDDLESEX SOUTH DISTRICT MEDICAL SOCIETY

August 1—Joint meeting with the Middlesex South District Medical Golf Association. See notice elsewhere on this page.